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Patents Form 1/77

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# Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

**The Patent Office**

Cardiff Road
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1. Your reference GBP86436

2. Patent application number
(The Patent Office will fill in this part) 0218816.7

3 Full name, address and postcode of the or of each applicant (underline all surnames)

Pharma Mar, S.A.,
Calle de la Calera 3
Poligono Industrial de Tres Cantos
Tres Cantos
E-28760 Madrid
Spain

Patents ADP number (if you know it) 4385114 1003

If the applicant is a corporate body, give the country/state of its incorporation Spain

4. Title of the invention ANTITUMORAL ANALOGS OF LAMELLARINS

5. Name of your agent (if you have one)
"Address for service" in the United Kingdom to which all correspondence should be sent
(including the postcode)

Marks & Clerk
57 - 60 Lincolns Inn fields
London WC2A 3LS

Patents ADP number (if you know it) 18001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number

| Country | Priority application No (if you know it) | Date of filing (day / month / year) |
|---|---|---|

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

| Number of earlier application | Date of filing (day / month / year) |
|---|---|

8. Is a statement of inventorship and of right to grant of a patent required in support ofthis request? (Answer 'Yes' if:
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d)) Yes

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| | |
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| Continuation sheets of this form | 0 |
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| Priority documents | |
| Translations of priority documents | |
| Statement of inventorship and right to grant of a patent (Patents Form 7/77) | |
| Request for preliminary examination and search (Patents Form 9/77) | |
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11. I/We request the grant of a patent on the basis of this application.

Signature Marks & Clerk Date: 13 August 2002

12. Name and daytime telephone number of person to contact in the United Kingdom

GB Patent Filings
0207 400 3000

Document : 849938

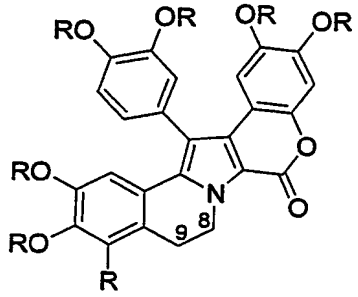
# ANTITUMORAL ANALOGS OF LAMELLARINS

## FIELD OF THE INVENTION

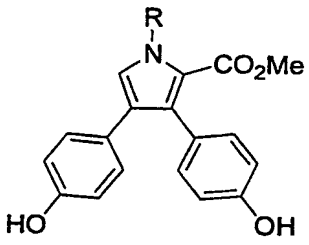
The present invention relates to antitumoral compounds, and in particular to new antitumoral analogs of lamellarins, pharmaceutical compositions containing them and their use in the treatment of cancer.

## BACKGROUND OF THE INVENTION

The lamellarins are polyaromatics alkaloids originally isolated from marine sources and comprising a fused polyaromatic framework. The family of lamellarins are constituted by two basic structures:

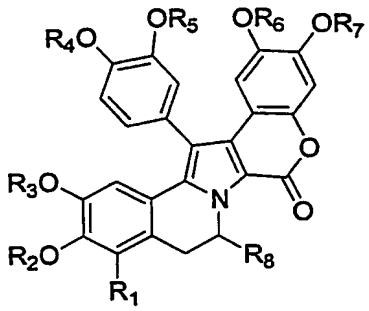



1

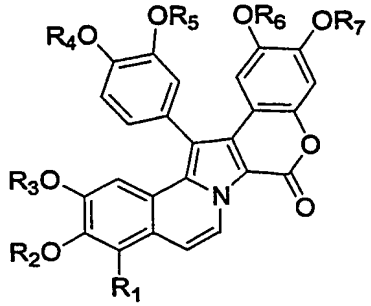



2

Both structures have a pirrolic ring substituted with aryl units. The hexacyclic structure 1 are a 14-phenyl-6*H*- [1]benzopiran[4',3',4,5] pyrrolo[2,1-*a*]isoquinolin-6-one. It depends of the substituents and the presence of a double bond between C8-C9 the members of this family are designed with different letters.




| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ | $R_7$ | $R_8$ |
|---|---|---|---|---|---|---|---|---|
| A | $OCH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_3$ | H | OH |
| C | $OCH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_3$ | H | H |
| E | OH | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | H | H |
| F | OH | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | H | H |
| G | H | H | $CH_3$ | $CH_3$ | H | H | $CH_3$ | H |
| I | $OCH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | H | H |
| J | H | H | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | H | H |
| K | OH | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_3$ | H | H |
| L | H | H | $CH_3$ | $CH_3$ | H | $CH_3$ | H | H |
| S | H | H | $CH_3$ | H | H | H | H | H |
| T | $OCH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | H | H |
| U | H | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | H | H |
| V | $OCH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | H | OH |
| Y | H | $CH_3$ | H | $CH_3$ | H | $CH_3$ | $SO_3Na$ | H |
| Z | H | H | $CH_3$ | H | H | H | $CH_3$ | H |
| β | H | H | H | $CH_3$ | H | H | H | H |



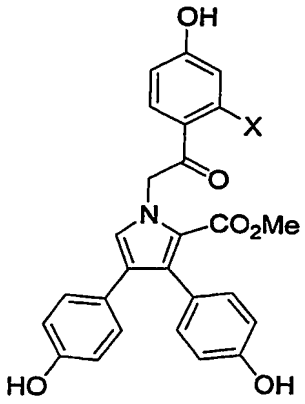

| | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | $R_6$ | $R_7$ |
|---|---|---|---|---|---|---|---|
| B | $OCH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_3$ | H |
| D | H | H | $CH_3$ | H | $CH_3$ | $CH_3$ | H |
| H | H | H | H | H | H | H | H |
| M | OH | $CH_3$ | $CH_3$ | H | $CH_3$ | $CH_3$ | H |
| N | H | H | $CH_3$ | $CH_3$ | H | $CH_3$ | H |
| W | $OCH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | H |
| X | OH | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | H |
| α | H | $CH_3$ | $CH_3$ | $CH_3$ | H | $CH_3$ | $SO_3Na$ |

R. J. Anderson et al, *J. Am. Chem. Soc.* **1985**, *107*, 5492, describes the isolation and characterization of four polyaromatic metabolites, the lamellarins A-D, obtained from a marine prosobranch mollusc *Lamellaria sp.* The structure of lamellarin A was determined by an X-Ray crystallographic study and the structures of lamellarins B-D were assigned by interpretation of spectral data.

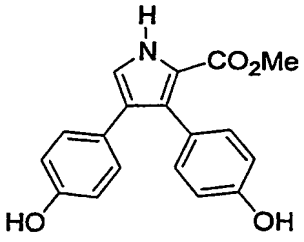
N. Lindquist et al, *J. Org. Chem.* **1988**, *53*, 4570, describes the isolation and characterization of four new lamellarins: E-H from the marine ascidian *Didemnum chartaceum* obtained from the Indian Ocean. The structure of lamellarin E was determined by an X-Ray crystallographic study.

A. R. Carroll et al, *Aust. J. Chem.* **1993**, *46*, 489, isolated six new lamellarins: I, J, K, L, M and the triacetate of the lamellarin N, and four known of this type: A, B, C, and the triacetate of lamellarin D, isolated from a marine ascidian *Didemnum sp.*

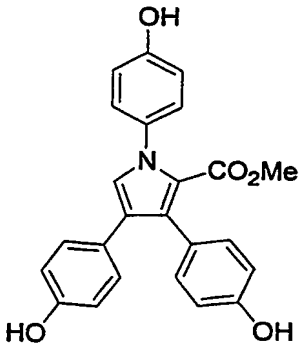
S. Urban et al, *Aust. J. Chem.* **1994**, *47*, 1919 and *Aust. J. Chem.* **1995**, *48*, 1491, described the isolation and characterization of four new lamellarins, O, P, Q, R, with the substructure type 2 from the marine sponge *Dendrilla cactos*. Latter S. Urban et al, *Aust. J. Chem.* **1996**, *49*, 711, described the structure of lamellarin S from the ascidian *Didemnum sp.*




O (X= H)
P (X= OH)




Q




R

M. V. R. Reddy et al, *Tetrahedron* **1997**, *53*, 3457, isolated five new lamellarins: T, U, V, W, and X, and the first example of sulfated lamellarin, Y, isolated from the marine ascidian *Didemnum sp* obtained from the Arabian sea.

R. A. Davis et al, *J. Nat. Prod.* **1999**, *62*, 419, described one new lamellarin, Z, and various examples of sulphated lamellarins isolated from the marine ascidian *Didemnum chartaceum*.

M. V. R. Reddy et al, *J. Med. Chem.* **1999**, *42*, 1901, isolated a new lamellarin, α, isolated from the marine ascidian *Didemnum sp.*

Finally, J. Ham et al, *Bull. Korean Chem. Soc.* **2002**, *23*, 163, described the isolation and characterization of the lamellarin β obtained from a marine ascidian *Didemnum sp.*

Lamellarins C and D have been shown to cause inhibition of cell division in a fertilised sea urchin assay, whereas lamellarins I, K , and L all exhibit comparable cytoxicity against P388 and A549 cell lines in culture. Recently, lamellarin N has been shown to exhibit activity in lung cancer cell lines by acting as a Type IV microtubule poison.

Furthermore, J. L. Fernández-Puentes et al, PCT Int. Appl WO 97/01336, describe that these compounds have also cytotoxic activity on multidrug resistant cells as well as efficacy as non-toxic modulators of the multidrug resistant phenotype and, therefore, afford an attractive potential source of chemotherapeutic agents.

The limited availability of natural material has resulted in the search for alternative synthetic methods being sought for the natural compounds and related analogs. W. Steglich et al, *Angew. Chem. Int. Ed. Eng.* **1997**, *36*, 155, have described a biomimetic sequence for the synthesis of lamellarin G trimethyl ether by a sequential double cyclization of a 1,3,4-triaryl-2,5-dicarboxysubstituted pyrrole ring. Following this strategy W. Steglich et al, *Chem. Eur. J.* **2000**, *6*, 1147, described the synthesis of lamellarin L.

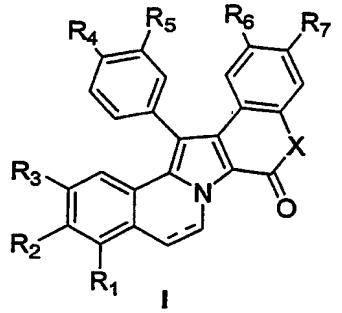
Another approach has included N-ylide-mediated pyrrole ring formation to install the pyrrole and lactone portions of the lamellarin. This strategy was followed by F. Ishibashi et al, *Tetrahedron* **1997**, *53*, 5951, to synthetise lamellarins D and H.

M. G. Banwell et al, *Chem. Commum.* **1997**, 2259; Int. Patent Appl. WO 98/50365 and Int. Patent Appl. WO 99/67250 described the synthesis of lamellarin K via 1,3-dipolar cycloaddition between an alkyne and an N-ylide of isoquinolin.

Ishibashi F. et al., *J.Nat.Prod.*, **2002**, 65, 500-504 describe the synthesis and structure activity relationship of lamellarin derivatives.

## SUMMARY OF THE INVENTION

The present invention is directed to compounds of the general formula I:




I

wherein X is selected from the group consisting of N, O and S;

wherein $R_1$, $R_2$, $R_3$, $R_4$, $R_5$, $R_6$ and $R_7$ are each independently selected from the group consisting of H, OH, OR', SH, SR', SOR', $SO_2R'$, NHR', $N(R')_2$, NHCOR', $N(COR')_2$, $NHSO_2R'$, OC(=O)H, OC(=O)R', $OCO_2H$, $OCO_2R'$, $C_1$-$C_{12}$ alkyl, $C_1$-$C_{12}$ haloalkyl, $C_2$-$C_{12}$ alkenyl, $C_2$-$C_{12}$ alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl and substituted or unsubstituted heteroaromatic;

wherein each of the R' groups is independently selected from the group consisting of H, OH, $NO_2$, $NH_2$, SH, CN, halogen, =O, C(=O)H, $C(=O)CH_3$,

$CO_2H$, substituted or unsubstituted $C_1$-$C_{24}$ alkyl, substituted or unsubstituted $C_2$-$C_{18}$ alkenyl, substituted or unsubstituted $C_2$-$C_{18}$ alkynyl, substituted or unsubstituted aryl;
and the dotted line represents an single or double bond.

Antitumoral activities of these compounds include leukaemias, lung cancer, colon cancer, kidney cancer, prostate cancer, ovarian cancer, breast cancer, sarcomas and melanomas.

In another aspect the present invention is directed to pharmaceutical compositions useful as antitumor agents that contain as active ingredient a compound or compounds of the invention, as well as the process for their preparation.

The present invention is also directed to the use compounds of the general formula **I** above in the treatment of cancer, or in the preparation of a medicament for the treatment of cancer.

**DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS.**

One class of preferred compounds of this invention includes compounds of this invention which have one or more of the following substituents:

$R_1$ is preferably H or OR' with R' preferably lower alkyl or aminoacid or small peptide.

Preferred R' groups are present in groups of formula R', COR' or OCOR' and include alkyl or alkenyl, that may be substituted at one or more available positions by one or more suitable groups, e.g., halogen such as fluoro, chloro, bromo and iodo, especially w-chloro or perfluoro; aminoalkyl groups such as groups having one or more N atoms and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms,

and especially including amino acid, notably glycine, alanine, arginine, asparagine, asparaginic acid, cystein, glutamine, glutamic acid, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine or valine, especially protected forms of such amino acids; carbocylic aryl having 6 or more carbons, particularly phenyl; and aralkyl such as benzyl; heterocyclic groups including heteroalicyclic and heteroaromatic groups, especially with 5 to 10 ring atoms of which 1 to 4 are heteroatoms, more preferably heterocyclic groups with 5 or 6 ring atoms and 1 or 2 heteratoms or with 10 ring atoms and 1 to 3 heteroatoms, the heterocyclic groups optionally being substituted with one or more of the subsitituents permitted for R' and especially amino such as dimethylamino or with keto.

Suitable halogen substituents in the compounds of the present invention include F, Cl, Br and I.

Alkyl groups preferably have from 1 to 24 carbon atoms. One more preferred class of alkyl groups has 1 to about 12 carbon atoms, yet more preferably 1 to about 8 carbon atoms, still more preferably 1 to about 6 carbon atoms, and most preferably 1, 2, 3 or 4 carbon atoms. Another more preferred class of alkyl groups has 12 to about 24 carbon atoms, yet more preferably 12 to about 18 carbon atoms, and most preferably 13, 15 or 17 carbon atoms. Methyl, ethyl and propyl including isopropyl are particularly preferred alkyl groups in the compounds of the present invention. As used herein, the term alkyl, unless otherwise modified, refers to both cyclic and noncyclic groups, although cyclic groups will comprise at least three carbon ring members.

Preferred alkenyl and alkynyl groups in the compounds of the present invention have one or more unsaturated linkages and from 2 to about 12 carbon atoms, more preferably 2 to about 8 carbon atoms, still more preferably 2 to about 6 carbon atoms, even more preferably 1, 2, 3

or 4 carbon atoms. The terms alkenyl and alkynyl as used herein refer to both cyclic and noncyclic groups, although straight or branched noncyclic groups are generally more preferred.

Preferred alkoxy groups in the compounds of the present invention include groups having one or more oxygen linkages and from 1 to about 12 carbon atoms, more preferably from 1 to about 8 carbon atoms, and still more preferably 1 to about 6 carbon atoms, and most preferably 1, 2, 3 or 4 carbon atoms.

Preferred alkylthio groups in the compounds of the present invention have one or more thioether linkages and from 1 to about 12 carbon atoms, more preferably from 1 to about 8 carbon atoms, and still more preferably 1 to about 6 carbon atoms. Alkylthio groups having 1, 2, 3 or 4 carbon atoms are particularly preferred.

Preferred alkylsulfinyl groups in the compounds of the present invention include those groups having one or more sulfoxide (SO) groups and from 1 to about 12 carbon atoms, more preferably from 1 to about 8 carbon atoms, and still more preferebly 1 to about 6 carbon atoms. Alkylsulfinyl groups having 1, 2, 3 or 4 carbon atoms are particularly preferred.

Preferred alkylsulfonyl groups in the compounds of the present invention include those groups having one or more sulfonyl ($SO_2$) groups and from 1 to about 12 carbon atoms, more preferably from 1 to about 8 carbon atoms, and still more preferably 1 to about 6 carbon atoms. Alkylsulfonyl groups having 1, 2, 3 or 4 carbon atoms are particularly preferred.

Preferred aminoalkyl groups include those groups having one or more primary, secondary and/or tertiary amine groups, and from 1 to about 12 carbon atoms, more preferably 1 to about 8 carbon atoms, still

more preferably 1 to about 6 carbon atoms, even more preferably 1, 2, 3 or 4 carbon atoms. Secondary and tertiary amine groups are generally more preferred than primary amine moieties.

Suitable heterocyclic groups include heteroaromatic and heteroalicyclic groups. Suitable heteroaromatic groups in the compounds of the present invention contain one, two or three heteroatoms selected from N, O or S atoms and include, e.g., coumarinyl including 8-coumarinyl, quinolinyl including 8-quinolinyl, pyridyl, pyrazinyl, pyrimidyl, furyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, indolyl, benzofuranyl and benzothiazol. Suitable heteroalicyclic groups in the compounds of the present invention contain one, two or three heteroatoms selected from N, O or S atoms and include, e.g., tetrahydrofuranyl, tetrahydropyranyl, piperidinyl, morpholino and pyrrolindinyl groups.

Suitable carbocyclic aryl groups in the compounds of the present invention include single and multiple ring compounds, including multiple ring compounds that contain separate and/or fused aryl groups. Typical carbocyclic aryl groups contain 1 to 3 separate or fused rings and from 6 to about 18 carbon ring atoms. Specifically preferred carbocyclic aryl groups include phenyl including substituted phenyl such as 2-substituted phenyl, 3-substituted phenyl, 2.3-substituted phenyl, 2.5-substituted phenyl, 2.3.5-substituted and 2.4.5-substituted phenyl, including where one or more of the phenyl substituents is an electron-withdrawing group such as halogen, cyano, nitro, alkanoyl, sulfinyl, sulfonyl and the like; naphthyl including 1-naphthyl and 2-naphthyl; biphenyl; phenanthryl; and anthracyl.

References herein to substituted R' groups in the compounds of the present invention refer to the specified moiety, typically alkyl or alkenyl, that may be substituted at one or more available positions by one or more suitable groups, e.g., halogen such as fluoro, chloro, bromo

and iodo; cyano; hydroxyl; nitro; azido; alkanoyl such as a C1-6 alkanoyl group such as acyl and the like; carboxamido; alkyl groups including those groups having 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms and more preferably 1-3 carbon atoms; alkenyl and alkynyl groups including groups having one or more unsaturated linkages and from 2 to about 12 carbon or from 2 to about 6 carbon atoms; alkoxy groups having those having one or more oxygen linkages and from 1 to about 12 carbon atoms or 1 to about 6 carbon atoms; aryloxy such as phenoxy; alkylthio groups including those moieties having one or more thioether linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; alkylsulfinyl groups including those moieties having one or more sulfinyl linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; alkylsulfonyl groups including those moieties having one or more sulfonyl linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; aminoalkyl groups such as groups having one or more N atoms and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; carbocylic aryl having 6 or more carbons, particularly phenyl (e.g., R being a substituted or unsubstituted biphenyl moiety); and aralkyl such as benzyl; heterocyclic groups including heteroalicyclic and heteroaromatic groups, especially with 5 to 10 ring atoms of which 1 to 4 are heteroatoms, more preferably heterocyclic groups with 5 or 6 ring atoms and 1 or 2 heteratoms or with 10 ring atoms and 1 to 3 heteroatoms.

Preferred compounds of this invention include those with one or more of the following definitions:

X is NH; and/or

at least one of R1 to R7 is:

O(C=O)R', where (C=O)R' is optionally protected amino acid, optionally protected oligopeptide, or where R' is alkyl or alkenyl substituted with aryl, cycloalkyl or heterocycle, or where R' is alkyl of 1 to 24 carbon

atoms, or where R' is aryl or heterocycle, or where R' is alkyl substitued with arylthio, or where R' is alkynyl;
OTf;
OSO2R' where R' is alkyl;
R' where R' is alkyl of 1 to 6 carbon atoms;
O(O)PR'2, where R' is alkyl;
nitro;
N=CR'2, where R' is aryl;
NH2;

Suitably 1, 2 or 3 of R1 to R7 takes one of these preferred meanings , and more typically R1, R4 and R7, or R2, R4 and R7, or R4 and R7. In most embodiments, the 2 or 3 groups are the same, but differing groups can be employed. The remaining groups R1 to R7 are then suitably hydrogen, hydroxy or methoxy, especially with the ditribution patterns shown in the compounds of the examples. These distribution patterns may be applied generally to the compounds of this invention.

The oligopeptide is suitably (aa)n, where aa is an amino acid, each aa is the same or different, and n is 2 to 10, suitably 2 to 5, more suitably 2, 3, or 4, especially 2.

Alkyl substituted with aryl is suitably an alkyl of 1 to 6 carbon atoms, especially 1 or 2 carbon atoms, substitituted with phenyl, especially ω-phenyl as in benzyl or phenethyl.

Alkyl substituted with cycloalkyl is suitably an alkyl of 1 to 6 carbon atoms, especially 1 or 2 carbon atoms, substitituted with cycloalkyl of 3 to 10 carbon atoms, especially 5 to 8, more especially 6 carbon atoms.

Alkyl substituted with heterocycle includes biotin.

Alkenyl substituted with aryl is suitably an alkenyl of 2 to 6 carbon atoms, especially 2 carbon atoms, substitituted with phenyl itself optionally substituted, as in p-methylcinnamic acid.

Alkyl substituted with arylthio includes optionally substituted phenylthioalkyl where the alkyl has 1 to 3 carbon atoms and substituents include halo especially p-fluoro.

O(C=O)R' where R' is aryl include optionally substituted phenyl where substituents include 1 or more halo especially four fluoro groups or two bromo groups.

O(C=O)R' where R' is heterocycle includes coumarinyacyl, as in coumarin-3-carboxyl, or 9H-fluorenacyl, as in 9H-fluoren-4-carboxyl, or phenylethynylnicotinic acid.

Alkyl with 1 to 6 carbon atoms is suitably straight or branched alkyl.

Alkyl with 1 to 24 carbon atoms is suitably straight or branched alkyl, especially alkyl of 1 to 10 carbon atoms or alkyl with 11 to 23 carbon atoms, more especially 13 to 19 carbon atoms.

Alkynyl suitably has 2 to 8, more especially 3 to 7, carbon atoms, as in pentyn-4-yl.

O(O)PR'2, where R' is alkyl suitably has alkyl of 1 to 3 carbon atoms.

OSO2R' where R' is alkyl suitably has methyl for the alkyl.

N=CR'2, where R' is aryl is suitably N=C(phenyl)2.

Protecting groups for the optionally protected amino acid or optionally protected oligopeptide include those recited in listed in WO 0069862.

Another especially preferred embodiment of the present invention is pharmaceutical compositions useful as antitumor agents which contain as active ingredient a compound or compounds of the invention, as well as the processes for their preparation.

Examples of pharmaceutical compositions include any solid (tablets, pills, capsules, granules etc.) or liquid (solutions, suspensions or emulsions) with suitable composition or oral, topical or parenteral administration.

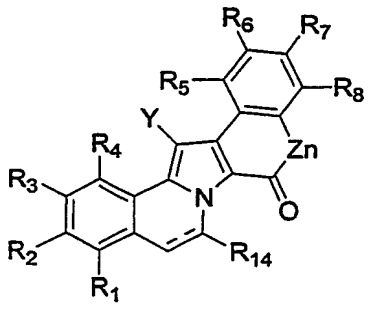
Administration of the compounds or compositions of the present invention may be any suitable method, such as intravenous infusion, oral preparation, intraperitoneal and intravenous preparation.

Administration of the compounds or compositions of the present invention may be by any suitable method, such as intravenous infusion, oral preparations, intraperitoneal and intravenous administration. We prefer that infusion times of up to 24 hours are used, more preferably 2-12 hours, with 2-6 hours most preferred. Short infusion times which allow treatment to be carried out without an overnight stay in hospital are especially desirable. However, infusion may be 12 to 24 hours or even longer if required. Infusion may be carried out at suitable intervals of say 2 to 4 weeks. Pharmaceutical compositions containing compounds of the invention may be delivered by liposome or nanosphere encapsulation, in sustained release formulations or by other standard delivery means.

The correct dosage of the compounds will vary according to the particular formulation, the mode of application, and the particular situs, host and tumour being treated. Other factors like age, body weight, sex, diet, time of administration, rate of excretion, condition of the host, drug combinations, reaction sensitivities and severity of the disease shall be taken into account. Administration can be carried out continuously or periodically within the maximum tolerated dose.

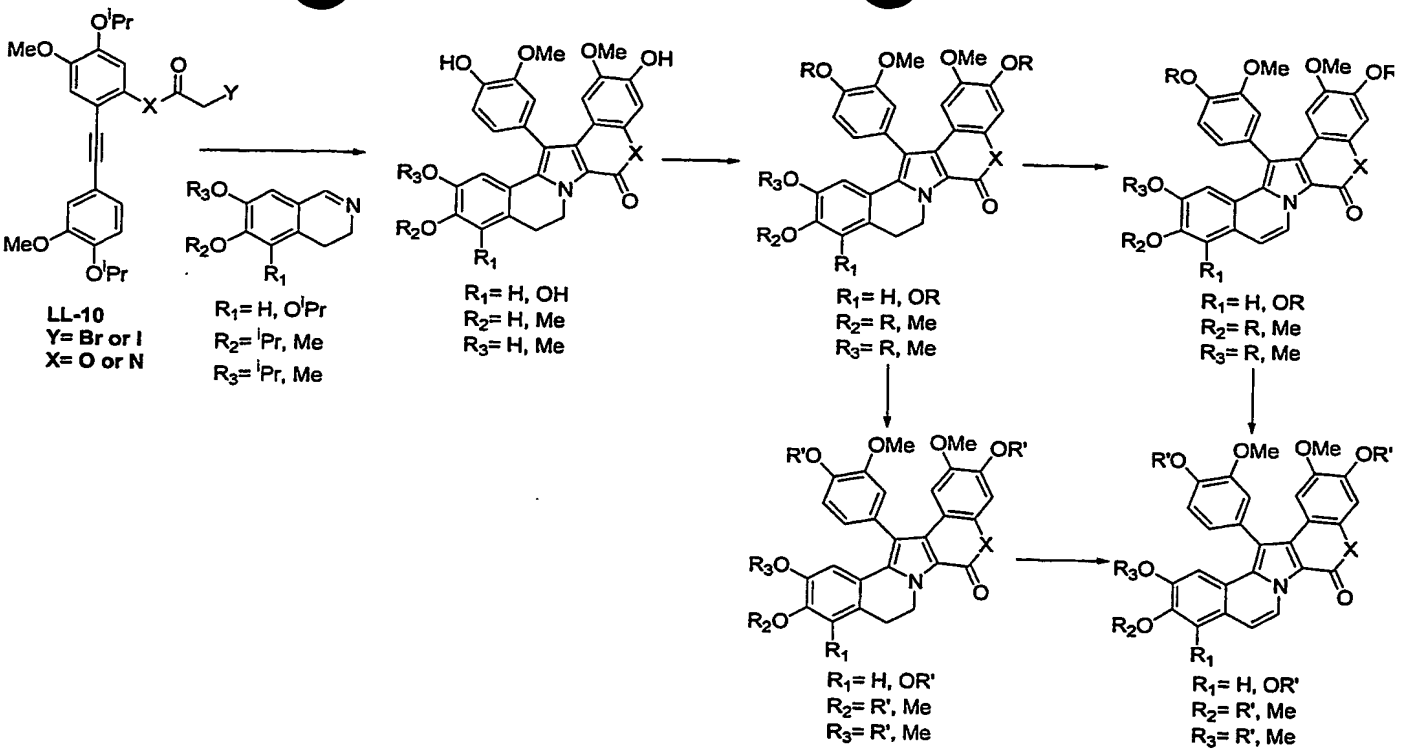
The compounds and compositions of this invention may be used with other drugs to provide a combination therapy. The other drugs may form part of the same composition, or be provided as a separate composition for administration at the same time or a different time.

The compound of the present invention can be prepared synthetically from the intermediate compound **Ia** described in the PCT Int. Appl WO 98/50365. Numerous active antitumoral compounds have been prepared from this compound and it is believed that many more compounds can be formed in accordance with the teachings of the present disclosure.




**Ia**

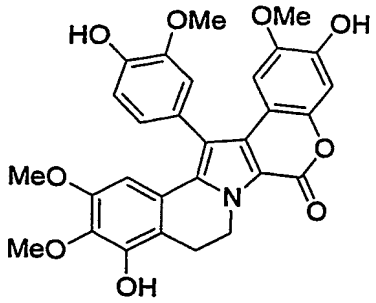
The compounds of the invention are prepared according to the following reaction scheme and the teaching of WO 98 50365.




## EXAMPLES

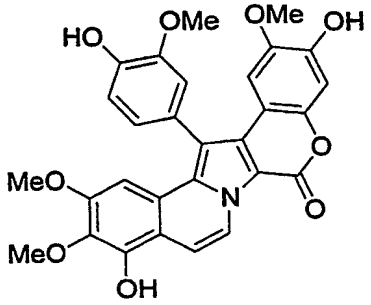
The experimental procedures and the physicochemical characteristics of some of the compounds of the invention are described hereinafter, examples of biological activities of the compounds of the present invention are included in tables at the end of the description. These examples are illustrative of the present invention and should not not be interpreted as limitative.

Example 1: Compound 1



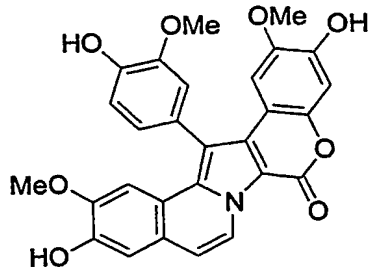
Aluminium chloride (1.26 g, 9.42 mmol) was added to a solution of **104** (1.55 g, 2.36 mmol) in anhydrous $CH_2Cl_2$ (50 mL) under Argon atmosphere. The reaction mixture was stirred for 6 h at 23 °C. After 2 and 4 h of reaction, anhydrous $CH_2Cl_2$ (2x20 mL) was added to get a successful stirring. The mixture was quenched with $CH_2Cl_2$:MeOH (20:1, 20 mL), silica gel (8.0 g) was added and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel ($CH_2Cl_2$:MeOH, from 20:1 to 15:1) to afford **1** as a pale brown solid (2.27 g, 95%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.13 (d, $J$= 7.8 Hz, 1H), 7.06 (dd, $J$= 7.8, 1.7 Hz, 1H), 6.98 (d, $J$= 1.7 Hz, 1H), 6.93 (s, 1H), 6.59 (s, 1H), 6.38 (s, 1H), 6.02 (s, 1H), 5.85 (s, 1H), 5.82 (s, 1H), 5.00-4.80 (m, 1 H), 4.70-4.50 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.49 (s, 3H), 3.36 (s, 3H), 3.20-3.00 (m, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.6, 150.3, 147.2, 146.3, 146.1, 145.5, 145.4, 143.3, 135.4, 135.3, 128.1, 127.3, 124.2, 123.2, 115.5, 115.1, 113.8, 113.4, 113.0, 110.1, 103.9, 103.3, 101.8, 61.0, 56.2, 55.6, 55.5, 42.0, 21.4. MS (ESI) m/z: 532 $(M+1)^+$. Rf: 0.30 ($CH_2Cl_2$:MeOH, 20:1).

Example 2: Compound **2**



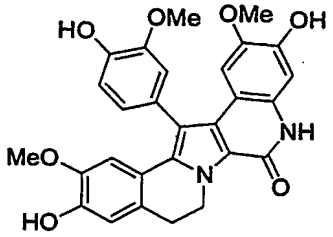

Aluminium chloride (10 mg, 0.079 mmol) was added to a solution of **27** (13 mg, 0.019 mmol) in anhydrous $CH_2Cl_2$ (1 mL) under Argon atmosphere. The reaction mixture was stirred for 3 h at 23 °C. The mixture was quenched with $CH_2Cl_2$:MeOH (20:1, 20 mL), silica gel (8.0 g) was added and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel ($CH_2Cl_2$:MeOH, from 20:1 to 10:1) to afford **2** as a pale brown solid (8 mg, 80%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.18 (d, $J$= 7.5 Hz, 1H), 7.40 (d, $J$= 7.5 Hz, 1H), 7.20-7.16 (m, 2H), 7.10 (s, 1H), 6.99 (s, 1H), 6.80 (s, 1H), 6.68 (s, 1H), 6.20 (br s, 1H), 5.80 (br s, 2H), 5.80 (br s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.52 (s, 3H), 3.46 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.5, 151.9, 147.3, 147.0, 146.3, 145.7, 144.5, 143.3, 134.8, 133.7, 129.3, 127.5, 124.7, 122.3, 121.4, 119.7, 115.2, 113.9, 113.8, 111.9, 109.8, 106.9, 104.6, 103.5, 98.3, 61.2, 56.3, 55.6, 55.1. MS (ESI) m/z: 529 $(M)^+$. Rf: 0.30 ($CH_2Cl_2$:MeOH, 20:1).

Example 3: Compound **3**



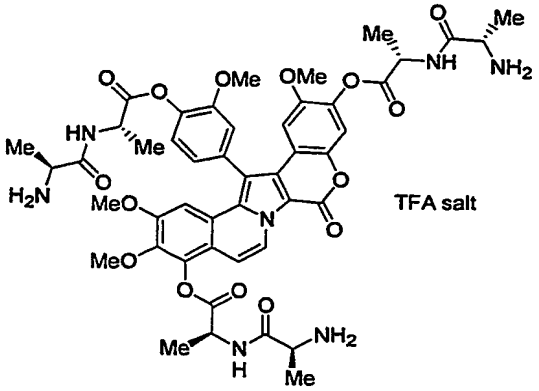
A suspension of **107** (271 mg, 0.433 mmol) and $AlCl_3$ (462 mg, 3.465 mmol) in anhydrous $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 5.5 h under Argon atmosphere. $H_2O$ was added, then HCl 2 M until pH 1-2, the resulting aqueous solution was extracted with $CH_2Cl_2$ (3x), dried over $Na_2SO_4$, filtered, and the solvent evaporated under reduced pressure. The residue was purified by chromatography on silica gel (EtOAc, 100%) to afford **3** as a pale yellow solid (92 mg, 43%). $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.92 (s, 1H), 9.81 (s, 1H), 9.,32 (s, 1H), 8.98 (d, $J$= 7.3 Hz, 1H), 7.22-6.98 (m, 6H), 6.85 (s, 1H), 6.70 (s, 1H), 3.75 (s, 3H), 3.36 (s, 6H). $^{13}C$ NMR (75 MHz, DMSO-$d_6$) $\delta$ 154.3, 148.7, 148.5, 148.3, 147.8, 146.8, 146.3, 144.6, 134.1, 129.2, 128.9, 125.5, 124.7, 123.9, 117.6, 116.4, 115.1, 113.9, 112.3, 111.5, 110.8, 106.4, 105.7, 105.4, 103.7, 56.0, 55.1, 54.5. MS (ESI) m/z: 500 $(M+1)^+$. Rf: 0.60 (ethyl acetate).

Example 4: Compound **4**




A suspension of **50** (15.0 mg, 0.024 mmol) and $AlCl_3$ (19.0 mg, 0.144 mmol) in anhydrous $CH_2Cl_2$ (2 mL) was stirred from 0 °C to 23 °C for 2 h under Argon atmosphere. MeOH (1 mL) was added and the solvent was evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 10:1) to provide **4** as a white solid (9.1 mg, 76%). $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.07-7.05 (m, 2H), 6.99-6.97 (m, 1H), 6.80 (br s, 2H), 6.75 (s, 1H), 6.71 (s, 1H), 4.75 (m, 1H), 3.82 (s, 3H), 3.43 (s 3H), 3.36 (s, 3H), 3.02 (br t, 2H). MS (ESI) m/z: 501 $(M+1)^+$. Rf: 0.32 ($CH_2Cl_2$:MeOH, 10:1).

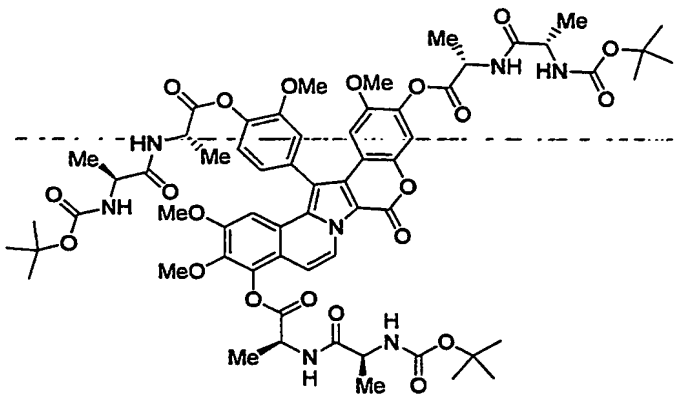
Example 5: Compound **5**




TFA (1 mL) was added to a solution of **6** (29 mg, 0.023 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **5** was obtained as a white solid (30 mg, quant.). The solid was collected by

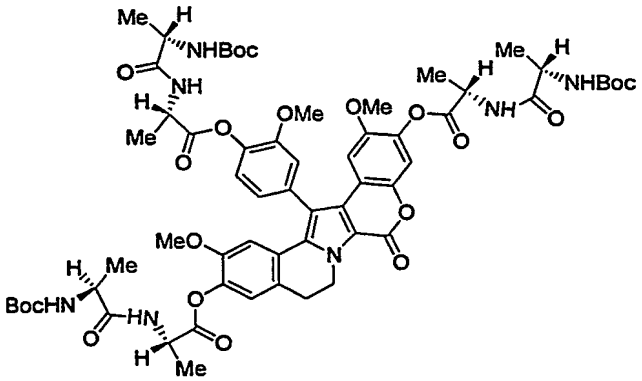
triturating in ethyl ether and filtrating. $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.07 (br s, 1H), 7.60-7.10 (m, 5H), 6.90-6.60 (m, 2H), 4.85-4.60 (m, 3H), 4.10-3.90 (m, 3H), 3.84 (s, 6H), 3.50 (s, 3H), 3.44 (s, 3H), 1.80-1.50 (m, 18H). MS (ESI) m/z: 956 $(M+1)^+$.

Example 6: Compound **6**



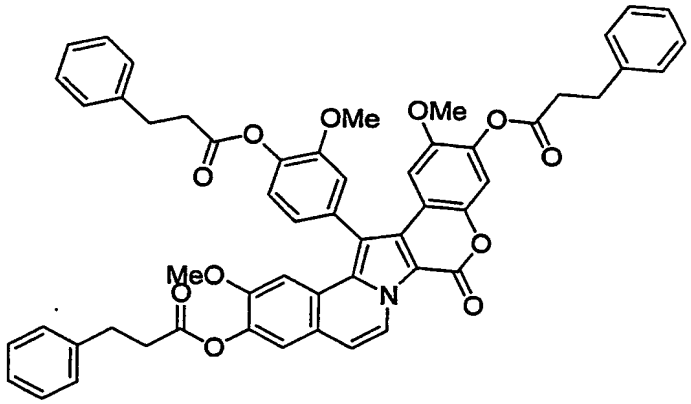
A suspension of **2** (27 mg, 0.051 mmol), Boc-Ala-Ala-OH (80 mg, 0.30 mmol), EDC·HCl (59 mg, 0.30 mmol) and DMAP (4 mg, 0.030 mmol) in $CH_2Cl_2$ (4 mL) was stirred under Argon atmosphere at 23 °C for 21 h. The resulting pale yellow solution was diluted with $CH_2Cl_2$, washed with $H_2O$, and HCl 0.1 N until pH=2 (2x20 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to give **6** as a white solid (56 mg, 87%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.02 (br s, 1H), 7.40-7.10 (m, 4H), 7.10-6.90 (m, 3H), 6.90-6.60 (m, 3H), 5.30-5.00 (m, 3H), 5.00-4.75 (m, 3H), 4.26 (br s, 3H), 3.85 (s, 6H), 3.47 (s, 3H), 3.43 (s, 3H), 1.80-1.30 (m, 45H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 173.1, 172.6, 171.3, 171.2, 171.1, 171.0, 170.9, 155.8, 154.8, 153.4, 153.3, 153.2, 152.4, 152.3, 147.6, 146.8, 145.5, 143.9, 141.8, 140.2, 140.0, 139.5, 138.9, 135.2, 134.8, 133.3, 133.2, 128.3, 128.2, 124.1, 123.8, 123.6, 121.1, 118.4, 115.9, 115.7, 115.5, 112.2, 111.9, 111.4, 109.1, 106.8, 106.4, 106.1, 104.5, 103.7, 80.5, 61.1, 56.6, 55.9, 55.8, 53.6, 50.2, 48.6, 48.4, 48.3, 28.5, 18.6, 18.3. MS (ESI) m/z: 1279 $(M+23)^+$. Rf: 0.24 ($CH_2Cl_2$:MeOH, 20:1).

Example 7: Compound **7**



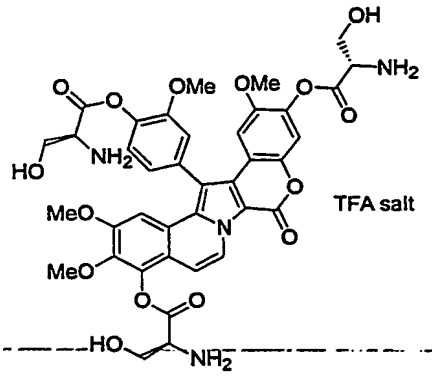
A suspension of **109** (25 mg, 0.050 mmol), Boc-Ala-Ala-OH (52 mg, 0.200 mmol), EDC·HCl (38 mg, 0.200 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$. (4.3 mL) was stirred under Argon atmosphere at 23 °C for 18 h. The resulting pale yellow solution was washed with $H_2O$, acidified with HCl until pH=2 (1x10 mL) and extracted with $CH_2Cl_2$ (1x10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to give **7** as a white solid (46 mg, 75%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.26-6.50 (m, 10H), 5.13-5.11 (m, 3H), 4.87-4.65 (m, 5H), 4.23 (bs, 3H), 3.78 (s, 3H), 3.39 (s, 3H), 3.32 (s, 3H), 3.06 (bt, 2H), 1.63-1.53 (m, 9H), 1.44-1.35 (m, 36H). MS (ESI) m/z: 1250 $(M+23)^+$. Rf: 0.40 ($CH_2Cl_2$:MeOH, 20:1).

Example 8: Compound **8**



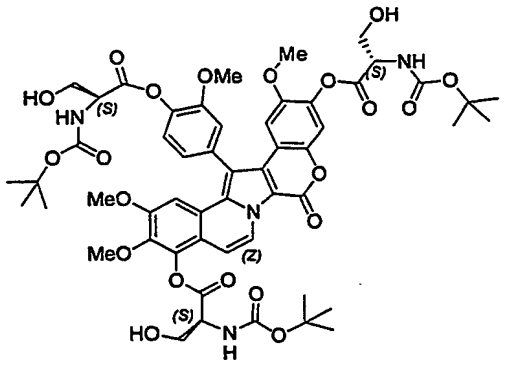

A suspension of **11** (23 mg, 0.026 mmol) and DDQ (12 mg, 0.051 mmol) in $CHCl_3$ (2 mL) was refluxed for 21 h. The mixture was cooled to 23 °C then filtered through Celite and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 100:1) to give **8** (16 mg, 70%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$= 7.3 Hz, 1H), 7.39-7.20 (m, 20H), 7.08-7.03 (m, 2H), 6.80 (s, 1H), 3.79 (s, 3H), 3.42 (s, 6H), 3.16-3.06 (m, 6H), 3.00-2.90 (m, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.8, 170.7, 170.6, 155.1, 152.4, 151.0, 147.7, 145.4, 140.9, 140.2, 140.1 (2C), 139.7, 134.2, 133.5, 128.5 (6C), 128.4 (2C), 128.4 (4C), 128.2, 126.4, 126.4 (2C), 124.0, 123.8, 123.6, 123.6, 123.1, 120.7, 115.6, 115.0, 112.8, 112.3, 112.1, 109.0, 106.4, 106.1, 56.2, 55.7, 55.6, 35.4 (3C), 30.9, 30.8 (2C). MS (ESI) m/z: 896 $(M+1)^+$. Rf: 0.25 ($CH_2Cl_2$:MeOH, 200:1).

Example 9: Compound **9**



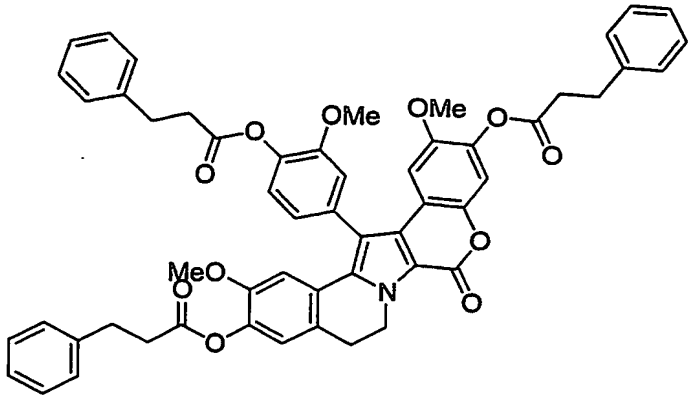

TFA (1 mL) was added to a solution of **10** (12 mg, 0.011 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **9** was obtained as a white solid (12 mg, quant.). The solid was collected by triturating in ethyl ether and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 9.15 (d, $J$= 7.5 Hz, 1H), 7.60-7.50 (m, 2H), 7.30-7.35 (m, 2H), 7.29 (s, 1H), 7.23 (s, 1H), 6.89 (s, 1H), 4.73 (br t, 1H), 4.54 (br t, 1H), 4.44 (br t, 1H), 4.30-4.10 (m, 6H), 3.89 (s, 6H), 3.54 (s, 3H), 3.47 (s, 3H). MS (ESI) m/z: 791 $(M+1)^+$.

Example 10: Compound **10**



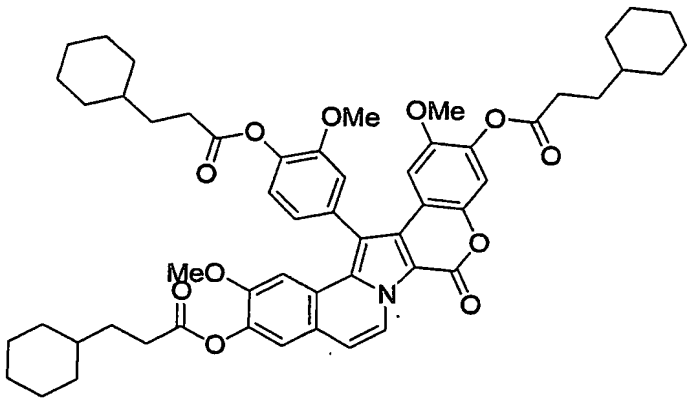

A suspension of **68** (35 mg, 0.025 mmol), Pd/C (4 mg, 10% weight) in methanol (1 mL) was purged three times successively with Argon/Vacuum. The mixture was stirred under $H_2$ atmosphere at 23 °C overnight at 1 atm. The reaction mixture was diluted with MeOH (5 mL), filtered over Celite, washed with MeOH:EtOAc (75 mL) and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 10:1) to give **10** as a white solid (23 mg, 82%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.05 (br s, 1H), 7.40-7.00 (m, 6H), 6.72 (d, $J$= 12.4 Hz, 1H), 5.70 (br s, 1H), 5.55 (br s, 2H), 4.90-4.60 (m, 3H), 4.32 (br s, 2H), 4.20-3.80 (m, 9H), 3.49 (s, 3H), 3.46 (s, 3H), 3.00-2.50 (m, 3H), 1.51 (s, 18H), 1.47 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.6, 169.2, 155.6, 154.5, 153.0, 151.7, 146.8, 145.5, 141.3, 139.8, 139.2, 138.7, 134.7, 133.0, 127.9, 124.0, 123.4, 120.9, 118.2, 115.8, 115.3, 112.1, 111.8, 108.9, 106.9, 106.2, 104.3, 80.6, 64.0, 63.7, 61.1, 56.5, 56.1, 55.8, 55.6, 28.3. MS (ESI) m/z: 1113 $(M+23)^+$, 1091 $(M+1)^+$. Rf: 0.30 ($CH_2Cl_2$:MeOH, 20:1).

Example 11: Compound 11




To a suspension of **109** (25 mg, 0.050 mmol) in $CH_2Cl_2$ (2 mL), 4-dimethylaminopyridine (4 mg, 0.030 mmol), pyridine (24 μL, 0.300 mmol) and hydrocinnamoyl chloride (45 μL, 0.300 mmol) were added. The reaction mixture was stirred under Argon atmosphere at 23 °C for 22 h, then diluted with ethyl acetate (50 mL) and washed with $H_2O$ (2x20 mL) and saturated aqueous solution of $NaHCO_3$ (2x20 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 200:1 to 100:1) to give **11** as a white solid (31 mg, 69%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.37-7.21 (m, 15H), 7.13-7.02 (m, 4H), 6.87 (s, 1H), 6.77 (s, 1H), 6.68 (s, 1H), 4.92-4.83 (m, 1H), 4.79-4.70 (m, 1H), 3.76 (s, 3H), 3.39 (s, 3H), 3.32 (s, 3H), 3.13-3.04 (m, 8H), 2.97-2.87 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 170.7, 170.6, 155.1, 152.2, 149.8, 147.7, 144.9, 140.1 (3C), 140.0, 139.4, 138.9, 135.0, 133.9, 128.5 (6C), 128.4 (6C), 127.1, 126.4, 126.4, 126.4, 125.9, 125.6, 123.8, 123.1, 122.6, 116.0, 115.9, 114.9, 114.6, 111.9, 109.7, 105.4, 56.1, 55.7, 55.5, 42.4, 35.5 (3C), 30.9, 30.9, 30.8, 28.0. MS (ESI) m/z: 898 $(M+1)^+$. Rf: 0.25 ($CH_2Cl_2$:MeOH, 200:1).

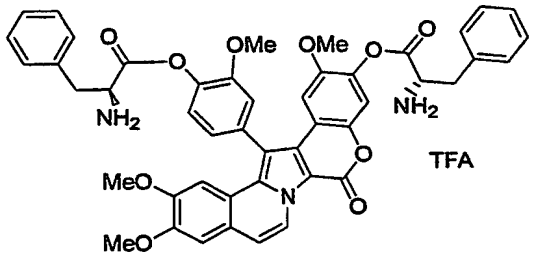
Example 12: Compound 12




A suspension of **106** (16 mg, 0.017 mmol) and DDQ (8 mg, 0.035 mmol) in $CHCl_3$ (2 mL) was refluxed for 17 h. The mixture was cooled to 23 °C then filtered through Celite and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH,

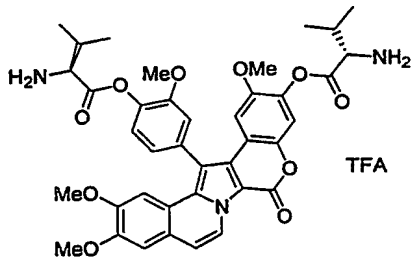
50:1) to give 12 (21 mg, quantitative). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$= 7.3 Hz, 1H), 7.38 (s, 1H), 7.29-7.13 (m, 5H), 7.06 (d, $J$= 7.5 Hz, 1H), 6.81 (s, 1H), 3.82 (s, 3H), 3.45 (s, 6H), 2.67-2.57 (m, 6H), 1.82 (m, 21H), 1.40-1.13 (m, 12H), 1.04-0.85 (m, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 172.0, 171.9 (2C), 155.1, 152.5, 151.1, 147.9, 145.5, 141.0, 140.4, 139.9, 134.1, 133.6, 128.3, 124.1, 123.8, 123.6, 123.1, 120.7, 115.6, 115.0, 112.8, 112.3, 112.2, 109.0, 106.4, 106.1, 56.2, 55.8, 55.7, 37.3 (3C), 37.1 (3C), 33.0 (6C), 32.3, 32.3, 32.2, 31.6 (3C), 26.5 (2C), 26.3 (2C), 26.3 (2C). MS (ESI) m/z: 914 $(M+1)^+$. Rf: 0.17 (hexane:EtOAc, 4:1).

Example 13: Compound 13



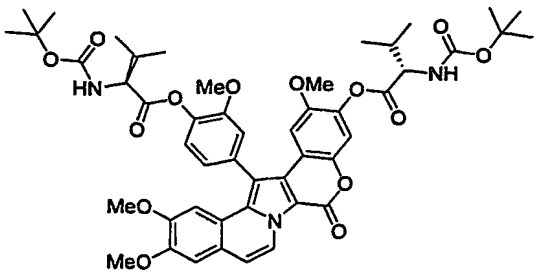

TFA (1 mL) was added to a solution of 58 (9.4 mg, 0.00932 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x2 mL) and evaporated to dryness to give 13 as a white solid (10.5 mg, quant). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 8.93 (d, $J$= 7.1 Hz, 1H), 7.58 (d, $J$= 7.8 Hz, 1H), 7.47-7.34 (m, 12H), 7.20 (s, 1H), 7.12 (d, $J$= 7.3 Hz, 1H), 7.08 (s, 1H), 7.0 (d, $J$= 4.0 Hz, 1H), 6.83 (s, 1H), 4.76 (br t, $J$= 6.8 Hz, 1H), 4.61 (m, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 3.46-3.31 (m, 7H). MS (ESI) m/z: 830.1 $(M+23)^+$, 808 $(M+1)^+$.

Example 14: Compound 14



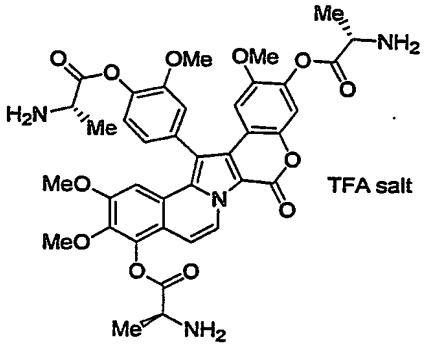

TFA (1 mL) was added to a solution of 15 (9.5 mg, 0.0104 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x2 mL) and evaporated to dryness to give 14 as a white solid (11.6 mg, quant). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.05 (m, 1H), 7.58-7.47 (m, 2H), 7.38-7.31 (m, 3H), 7.38-7.10 (m, 4H), 6.88 (br d, 1H), 4.36 (m, 1H), 4.25 (m,2H), 3.92 (s, 3H), 3.88 (s, 3H), 3.47 (s, 6H), 2.50-2.48 (m, 2H), 1.27 (d, $J$= 6.1 Hz, 6H), 1.20 (, $J$= 6.8 Hz, 6H). MS (ESI) m/z: 712 $(M+1)^+$.

Example 15: Compound 15



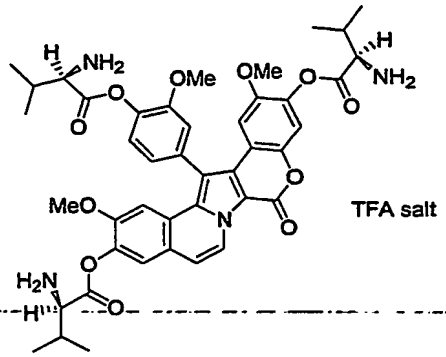
A suspension of 65 (32.4 mg, 0.0354 mmol) and DDQ (12.1 mg, 0.0532 mmol) in $CHCl_3$ (2 mL) was heated at 65 °C for 20 h under Argon atmosphere. The reaction mixture was filtered throught Celite, washed with $CH_2Cl_2$ (50 mL), and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give 15 as a white solid (29.0 mg, 90%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.20 (d, $J$= 7.6 Hz, 1H), 7.32-7.23 (m, 3H), 7.12-7.05 (m, 4H), 6.80 (d, $J$= 9.2 Hz, 1H), 5.09 (br d, 2H), 4.52 (br s, 2H), 3.98 (s, 3H), 3.80 (s, 3H), 3.50 (s, 3H), 3.43 (s, 3H), 2.43-2.37 (m, 2H), 1.49 (s, 9H9, 1.46 (s, 9H), 1.14-0.99 (m, 12H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.4, 155.7 (2C), 154.9, 152.2, 150.3, 149.6, 147.5, 145.5, 139.9, 139.3, 134.8, 134.2, 128.3, 128.2, 124.7, 123.9 (2C), 123.1, 118.9, 116.0, 115.3, 113.0, 112.1, 110.9, 108.4, 107.4, 106.2, 105.1, 80.0 (2C), 58.6 (2C), 56.0, 55.9, 55.7, 55.6, 31.3, 31.2, 28.3 (9C), 19.2, 19.0, 17.1 (2C). MS (ESI) m/z: 934.2 $(M+23)^+$, 912 $(M+1)^+$. Rf: 0.54 ($CH_2Cl_2$:MeOH, 60:1).

Example 16: Compound 16



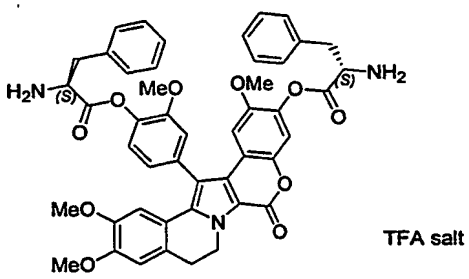

TFA (1 mL) was added to a solution of 97 (30 mg, 0.028 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness 16 was obtained as a white solid (31 mg, quant.). The solid was collected by triturating in ethyl ether and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 9.11 (dd, $J$= 7.5, 2.3 Hz, 1H), 7.60-7.50 (m, 2H), 7.35 (t, $J$= 6.6 Hz, 1H), 7.25-7.20 (m, 3H), 6.86 (d, $J$= 9.5 Hz, 1H), 4.66 (q, $J$= 7.3 Hz, 1H), 4.52 (q, $J$= 7.3 Hz, 1H), 4.38 (q, $J$= 7.1 Hz, 1H), 3.90 (d, $J$= 3.2 Hz, 3H), 3.89 (d, $J$= 1.8 Hz, 3H), 3.53 (d, $J$= 2.7 Hz, 3H), 3.47 (s, 3H), 1.85 (d, $J$= 7.0 Hz, 3H), 1.80 (d, $J$= 7.1 Hz, 3H), 1.69 (dd, $J$= 7.1, 4.0 Hz, 3H). MS (ESI) m/z: 743 $(M+1)^+$.

Example 17: Compound 17



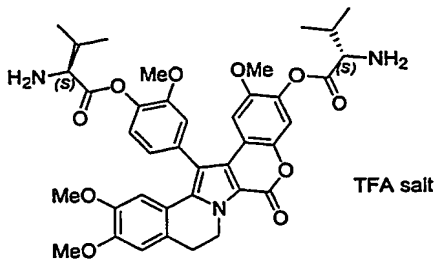

TFA (1 mL) was added to a solution of 122 (15 mg, 0.014 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give 17 as a white solid (21 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.13-9.09 (m, 1H), 7.63-7.52 (m, 3H), 7.44-7.22 (m, 4H), 6.89 (d, $J$ =9.2 Hz, 1H), 4.36 (d, $J$ =4.4 Hz, 1H), 4.32 (d, $J$ =4.0 Hz, 1H), 4.25 (t, $J$ =3.8 Hz, 1H), 3.91 (s, 3H), 3.48 (s, 6H), 2.61-2.44 (m, 3H), 1.29-1.19 (m, 18H). MS (ESI) m/z: 797 $(M+1)^+$.

Example 18: Compound 18



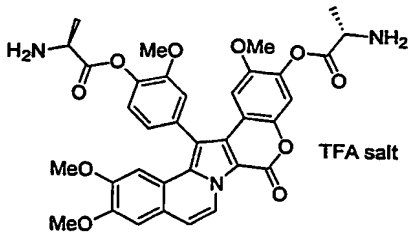

TFA (1 mL) was added to a solution of 84 (20.0 mg, 0.0233 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x2 mL) and evaporated to dryness to give 18 as a white solid (21.6 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.44-7.37 (m, 11H), 7.23-7.20 (m, 2H), 7.03 (s, 1H), 6.90 (s, 1H), 6.78 (m, 1H), 6.67 (s, 1H), 4.72-4.60 (m, 4H), 3.90 (s, 3H), 3.81 (s, 3H), 3.44 (s, 3H), 3.39-3.30 (m, 4H), 3.11 (br t, 2H). MS (ESI) m/z: 810 $(M+1)^+$.

Example 19: Compound 19



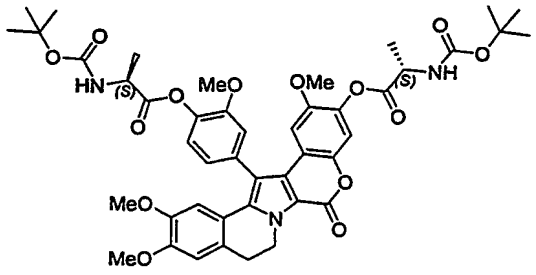
TFA (1 mL) was added to a solution of **65** (20.0 mg, 0.0233 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x2 mL) and evaporated to dryness to give **19** as a white solid (43.3 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.43-7.40 (m, 2H), 7.25-7.17 (m, 3H), 6.94 (br s, 1H), 6.80 (d, $J$= 13.4 Hz, 1H), 6.69 (d, $J$= 9.03 Hz, 1H), 4.90 (m, 2H), 4.32 (m, 1H), 4.22 (m, 2H), 3.86 (s, 3H), 3.45 (s, 3H), 3.36 (s, 3H), 3.13 (br t, 2H), 2.58-2.40 (m, 2H), 1.25 (br d, 6H), 1.17 (br d, 6H). MS (ESI) m/z: 736.1 $(M+23)^+$, 714 $(M+1)^+$.

Example 20: Compound **20**




TFA (1 mL) was added to a solution of **77** (9.7 mg, 0.0113 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x2 mL) and evaporated to dryness to give **20** as a white solid (11.7 mg, quant). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.03 (d, $J$= 7.3 Hz, 1H), 7.57-7.48 (m, 2H), 7.37-7.32 (m, 1H), 7.26-7.25 (m, 1H), 7.21-7.20 (m, 2H), 7.11 (d, $J$= 6.8 Hz, 1H), 6.87 (d, $J$= 8.3 Hz, 1H), 4.52 (br q, $J$= 6.8 Hz, 1H), 4.42 (br q, $J$= 6.8 Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.48 (s, 6H), 1.85 (d, $J$= 7.3 Hz, 1H), 1.71 (d, $J$= 7.1 Hz, 1H). MS (ESI) m/z: 678.0 $(M+23)^+$, 656 $(M+1)^+$.

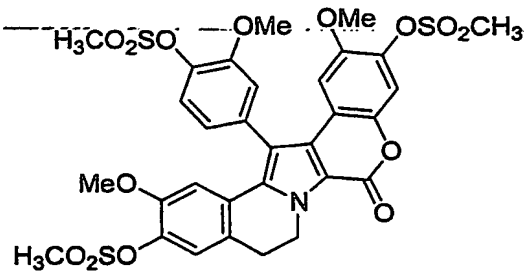
Example 21: Compound **21**




A suspension of **95** (50.0 mg, 0.097 mmol), (L)-N-Boc-alanine (73.4 mg, 0.388 mmol), EDC·HCl (74.4 mg, 0.388 mmol) and DMAP (5.0 mg, 0.04 mmol) in anhydrous $CH_2Cl_2$ (10 mL) was stirred at 23 °C for 3 h under Argon atmosphere. The reaction mixture was diluted with EtOAc (50 mL) and washed with $H_2O$ (50 mL) and with saturated aqueous solution of $NaHCO_3$ (50 mL), dried over $Na_2SO_4$, filtered, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give **21** as a white solid (83.2 mg, 100%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.23 (br s, 1H), 7.16-1.10 (m, 3 H), 6.76 (s, 1H), 6.71-6.56 (m,

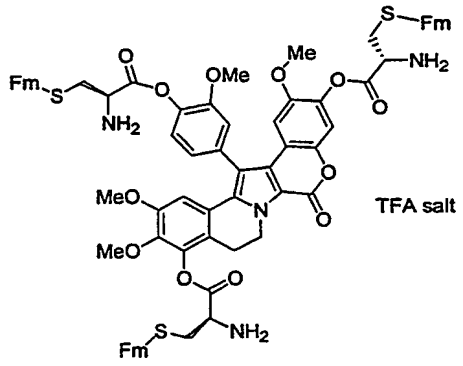
2H), 5.1 (m, 1H), 4.92-4.70 (m, 2H), 4.60-4.58 (m, 2H), 3.89 (s, 3H), 3.78 (s, 3H), 3.41 (s, 3H), 3.40 (s, 3H), 3.13 (t, $J$= 7.1 Hz, 2H), 1.63-1.46 (m, 24H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.3, 154.9, 151.9, 149.1, 147.6, 147.3, 144.8, 139.6, 138.4, 135.8, 134.4, 127.0, 126.4, 123.6, 123.3, 119.5, 116.2, 114.8, 114.6, 114.3, 111.6, 110.9, 108.4, 105.4, 79.9 (2C), 56.1, 55.8, 55.7, 55.3, 49.3 (2C), 42.4, 28.4, 28.2 (6C), 18.5 (2C). MS (ESI) m/z: 881 $(M+23)^+$, 859 $(M+1)^+$. Rf: 0.15 ($CH_2Cl_2$:MeOH, 60:1).

Example 22: Compound 22




To a suspension of **109** (50 mg, 0.0997 mmol) in anhydrous $CH_2Cl_2$ (2 mL) under Argon at 0 °C, $Et_3N$ (83 µL, 0.5982 mmol) and methanesulfonyl chloride (47 µL, 0.5982 mmol) were added. The resulting mixture was stirred at 23 °C for 6 h, then quenched with $H_2O$ and extracted with $CH_2Cl_2$ (3x20 mL). The combined organic layers were washed with saturated aqueous solution of $NaHCO_3$, dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, 80:1) to afford **22** as a pale yellow solid (47 mg, 64%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.52 (d, $J$= 8.1 Hz, 1H), 7.30 (s, 1H), 7.23-7.20 (m, 2H), 7.17 (d, $J$= 1.6 Hz, 1H), 6.75 (s, 1H), 6.65 (s, 1H), 4.99-4.90 (m, 1H), 4.71-4.61 (m, 1H), 3.92 (s, 3H), 3.46 (s, 3H), 3.38 (s, 3H), 3.34 (s, 3H), 3.19 (s, 3H), 3.18 (s, 3H), 3.14 (t, $J$= 6.0 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 154.5, 152.8, 150.1, 148.0, 144.6, 138.0, 137.7, 136.9, 135.4, 134.4, 126.5, 126.4, 126.3, 125.6, 124.4, 123.3, 117.0, 115.8, 115.4, 115.2, 113.5, 109.9, 105.6. MS (ESI) m/z: 736 $(M+1)^+$. Rf: 0.33 ($CH_2Cl_2$:MeOH, 80:1).

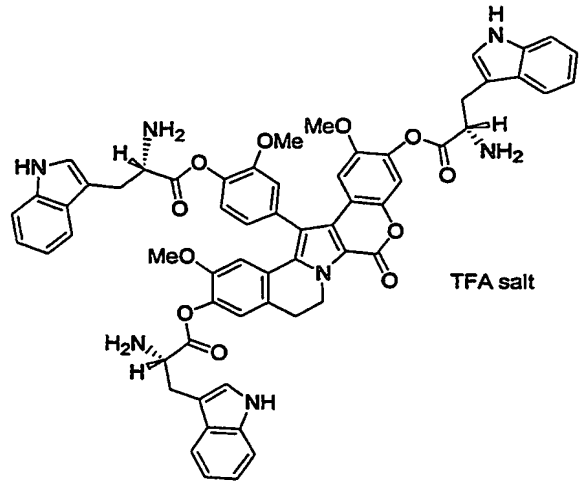
Example 23: Compound 23




TFA (1 mL) was added to a solution of **114** (19 mg, 0.011 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **23** was obtained as a white solid (20 mg, quant.). The solid was collected by

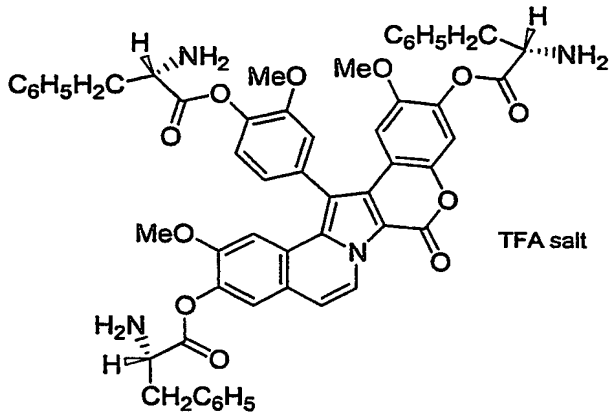
triturating and filtrating in ethyl ether. $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.90-7.60 (m, 12H), 7.45-7.20 (m, 16H), 6.80-6.70 (m, 2H), 4.80-4.40 (m, 5H), 4.35-4.20 (m, 3H), 3.74 (d, $J$= 2.9 Hz, 3H), 3.71 (d, $J$= 2.3 Hz, 3H), 3.55-3.30 (m, 12H) 3.35-3.00 (m, 6H), 2.91 (br s, 2H). MS (ESI) m/z: 1375 $(M)^+$.

Example 24: Compound 24




TFA (1 mL) was added to a solution of 29 (25 mg, 0.018 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1.5 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give 24 as a white solid (27 mg, quant.) $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.68 (d, $J$= 8.1 Hz, 1H), 7.62 (s, 1H), 7.60 (s, 1H), 7.44 (s, 1H), 7.42 (s, 3H), 7.34 (s, 1H), 7.30 (s, 1H), 7.29 (s, 1H), 7.21-7.16 (m, 5H), 7.12-7.09 (m, 3H), 6.98 (s, 1H), 6.85 (d, $J$= 2.0 Hz, 1H), 6.77-6.76 (m, 2H), 4.73-4.69 (m, 3H), 4.60 (br t, 2H), 3.87 (s, 3H), 3.77-3.34 (m, 6H), 3.43 (s, 3H), 3.34 (s, 3H). MS (ESI) m/z: 1060 $(M+1)^+$.

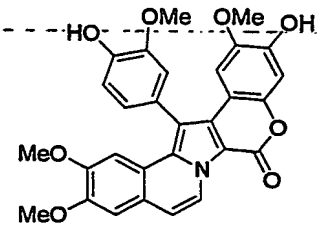
Example 25: Compound 25




TFA (1 mL) was added to a solution of 113 (15 mg, 0.012 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining

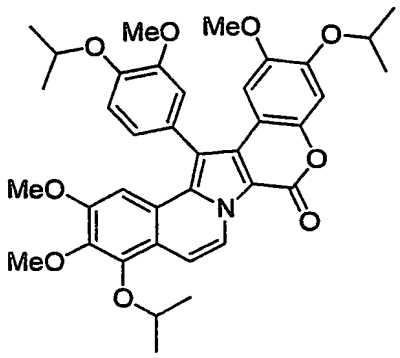
TFA, the mixture was treated with $CH_2C_{12}$ (3x15 mL) and evaporated to dryness to give 25 as a white solid (20 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.08 (d, $J$= 7.5 Hz, 1H), 7.60 (d, $J$= 2.2 Hz, 1H), 7.53 (s, 1H), 7.49-7.36 (m, 17H), 7.30 (d, $J$= 3.5 Hz, 1H), 7.20 (d, $J$= 7.5 Hz, 1H), 7.08 (d, $J$= 4.8 Hz, 1H), 6.87 (d, $J$= 4.2 Hz, 1H), 4.76 (t, $J$= 7.0 Hz, 1H), 4.70 (t, $J$= 6.9 Hz, 1H), 4.63 (t, $J$= 6.2 Hz, 1H), 3.95 (s, 3H), 3.47 (s, 6H), 3.61-3.36 (m, 6H). MS (ESI) m/z: 941 $(M+1)^+$.

Example 26: Compound 26




A suspension of 111 (165.5 mg, 0.2769 mmol) and $AlCl_3$ (147.7 mg, 1.1076 mmol) in anhydrous $CH_2Cl_2$ (5 mL) was stirred from 0 °C to 23 °C for 2 h under Argon atmosphere. MeOH (1 mL) was added and the solvent was evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to afford the compound which was purified again by chromatography on silica gel (EtOAc) to give 26 as a white solid (116 mg, 82%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.19 (d, $J$= 7.3 Hz, 1H), 7.19-6.98 (m, 7H), 6.71 (s, 1H), 5.86-5.85 (br s, 2H), 3.97 (s, 3H), 3.90 (s, 3H), 3.52 (s, 3H), 3.48 (s, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 154.2, 149.7, 148.7, 148.6, 147.7, 146.8, 146.3, 144.4, 133.5, 128.7, 125.5, 124.2, 124.0, 121.9, 118.2, 116.2, 115.2, 112.2, 110.8, 108.3, 107.7, 106.5, 105.6, 104.8, 103.6, 56.0, 55.4, 55.0, 54.4. MS (ESI) m/z: 536 $(M+23)^+$, 514 $(M+1)^+$. Rf: 0.45 ($CH_2Cl_2$:MeOH, 20:1).

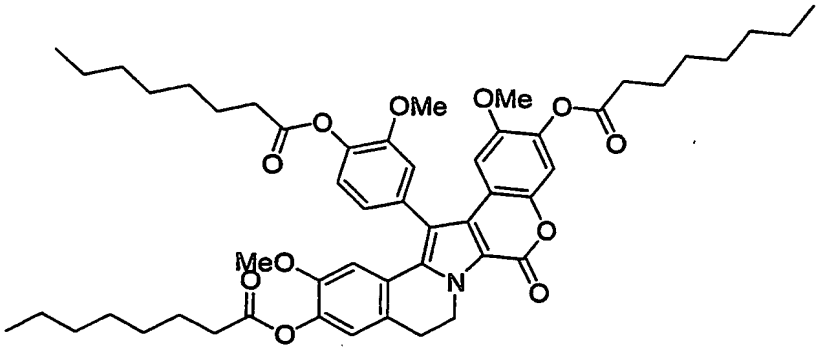
Example 27: Compound 27




LL-10-Br (155 mg, 0.31 mmol) was added in one portion to a solution of isoquinoline (78 mg, 0.31 mmol) in anhidrous DMA (2 mL) under Argon atmosphere. The solution was stirred at 23 °C for 19 h, then triethylamine (0.048 mL) was added and the reaction mixture was heated at 80 °C for 20 h. The reaction mixture was cooled, saturated aqueous solution of $NaHCO_3$ (0.5 mL) was added followed by addition of $(KSO_3)_2NO$ (85 mg, 0.31 mmol) and the mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ and extrated with $CH_2Cl_2$

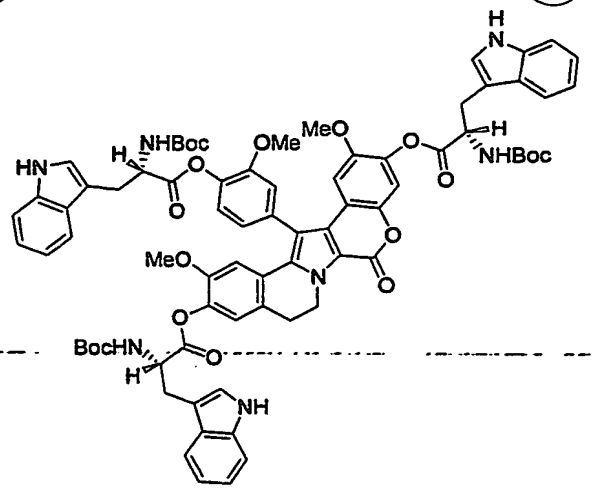
(4x20 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel (hexane:EtOAc, from 3:1 to 2:1) to afford **27** as a white solid (15 mg, 7%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.20 (d, $J$= 7.5 Hz, 1H), 7.43 (d, $J$= 7.6 Hz, 1H), 7.20-7.15 (m, 3H), 7.01 (s, 1H), 6.97 (s, 1H), 6.72 (s, 1H), 4.75-4.50 (m, 3H), 4.65-4.50 (m, 3H), 3.90 (s, 3H), 3.85 (s, 3H), 3.44 (s, 3H), 1.50-1.35 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 159.3, 155.6, 153.2, 151.4, 147.8, 147.2, 146.6, 146.5, 146.4, 142.5, 133.8, 129.3, 128.7, 123.8, 122.6, 121.3, 120.8, 116.9, 114.9, 111.9, 109.9, 107.7, 105.4, 103.4, 101.4, 76.4, 71.8, 71.4, 60.7, 56.2, 55.4, 55.1, 22.7, 21.9, 21.8. MS (ESI) m/z: 656 $(M+1)^+$. Rf: 0.20 (hexane:EtOAc, 2:1).

Example 28: Compound **28**



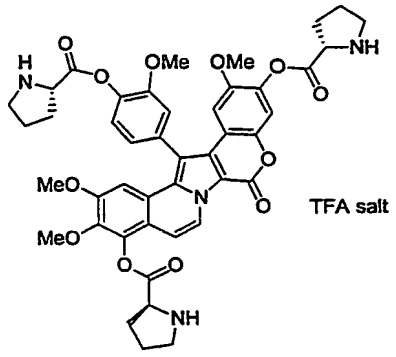

A suspension of **109** (25 mg, 0.050 mmol), *n*-octanoic acid (32 µL, 0.200 mmol), EDC·HCl (38 mg, 0.200 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 3 h. The resulting pale yellow solution was washed with $H_2O$ (1x10 mL) and saturated aqueous solution of $NaHCO_3$ (1x10 mL) and both aqueous phases were extracted with $CH_2Cl_2$ (1x10 mL). The combined organic layers were dried over $Na_2SO4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 100:1) to give **28** as a white solid (42 mg, 95%).$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.21-7.07 (m, 4H), 6.94 (s, 1H), 6.79 (s, 1H), 6.70 (s, 1H), 4.93-4.84 (m, 1H), 4.79-4.70 (m, 1H), 3.80 (s, 3H), 3.42 (s, 3H), 3.35 (s, 3H), 3.11 (t, $J$= 6.6 Hz, 2H), 2.63-2.53 (m, 6H), 1.83-1.69 (m, 6H), 1.41-1.30 (m, 24H), 0.93-0.87 (m, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.9, 171.6, 171.5, 155.1, 152.3, 149.9, 147.7, 144.9, 140.1, 139.5, 139.1, 135.1, 133.8, 127.1, 125.9, 125.5, 123.9, 123.1, 122.6, 115.9, 114.9, 114.6, 111.9, 109.7, 105.4, 56.1, 55.7, 55.5, 42.4, 34.0 (3C), 31.7 (3C), 29.0 (2C), 28.9 (4C), 28.0, 25.0 (2C), 24.9, 22.6 (3C), 14.0 (3C). MS (ESI) m/z: 902 $(M+23)^+$, 880 $(M+1)^+$. Rf: 0.31 ($CH_2Cl_2$:MeOH, 100:1).

Example 29: Compound **29**



A suspension of **109** (50 mg, 0.0997 mmol), Boc-L-Trp-OH (121 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 4 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and aqueous satures solution of $NaHCO_3$ (10 mL). The combined aqueous phases were extracted with $CH_2Cl_2$ (10mL). The combiend organic layers were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 30:1 to 15:1) to give **29** as a white solid (115 mg, 85%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.35 (s, 1H), 8.28 (s, 2H), 7.68-7-62 (m, 3H), 7.39-7.36 (m, 3H), 7.26-7.07 (m, 12H), 6.90 (s, 1H), 6.72 (s, 1H), 6.65 (br s, 2H), 5.15-5.12 (m, 2H), 5.00-4.59 (m, 6H), 3.75 (s, 3H), 3.52-3.28 (m, 12H), 3.00 (br t, 2H), 1.43 (s, 27H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.7, 170.4, 170.4, 155.3 (2C), 154.9,152.0, 149.6, 147.5, 144.6, 139.6, 139.0, 138.4, 136.1 (3C), 134.9, 134.0, 127.7 (3C), 126.8, 125.9, 125.5, 123.8, 123.1 (3C), 122.5, 122.0 (3C), 119.5 (3C), 118.6 (3C), 116.0, 115.8, 114.7, 111.7, 111.3 (3C), 109.5 (3C), 105.3, 80.0 (3C), 56.0 (2C), 55.6, 55.4, 54.4 (2C), 42.3, 28.2 (12C), 27.7. MS (ESI) m/z: 1382 $(M+23)^+$. Rf: 0.13 ($CH_2Cl_2$:MeOH, 30:1).

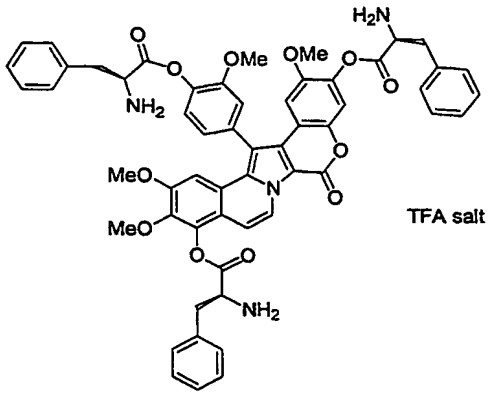
Example 30: Compound **30**




TFA (1 mL) was added to a solution of **117** (11 mg, 0.009 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **30** was obtained as a white solid (11 mg, quant.). The solid was collected by

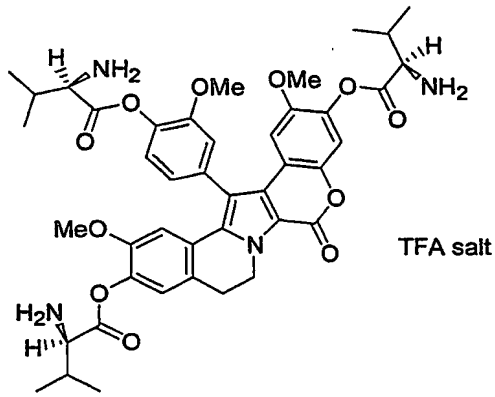
triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 9.15 (d, $J$= 7.6 Hz, 1H), 7.65-7.55 (m, 2H), 7.50-7.20 (m, 4H), 6.87 (d, $J$ = 12.3 Hz, 1H), 4.90-4.70 (m, 3H), 3.90 (s, 6H), 3.85-3.40 (m, 12H), 2.90-2.00 (m, 12H). MS (ESI) m/z: 821 $(M+1)^+$.

Example 31: Compound 31



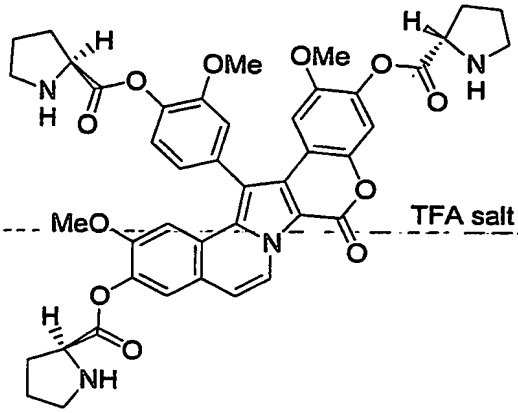

TFA (1 mL) was added to a solution of 120 (31 mg, 0.024 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness 31 was obtained as a white solid (31 mg, quant.). The solid was collected by triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 9.09 (d, $J$= 7.8 Hz, 1H), 7.80-7.40 (m, 18H), 7.30-7.00 (m, 3H), 6.87 (d, $J$= 5.3 Hz, 1H), 4.80-4.60 (m, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.80-3.40 (m, 12H). MS (ESI) m/z: 971 $(M)^+$.

Example 32: Compound 32



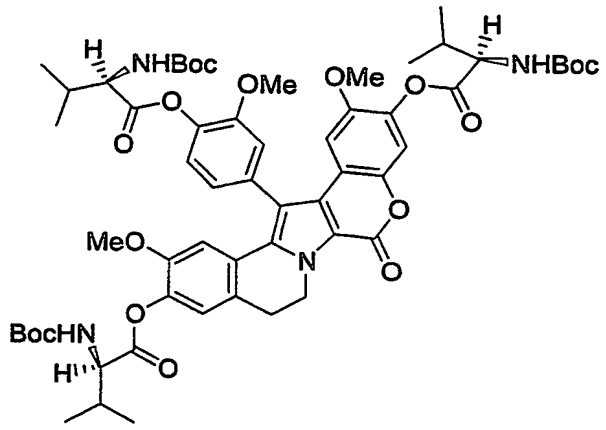

TFA (1 mL) was added to a solution of 34 (15 mg, 0.014 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give 32 as a white solid (19 mg, quant.). $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.46-7.44 (m, 2H), 7.29-7.25 (m, 1H), 7.17-7.14 (m, 2H), 6.90-6.78 (m, 2H), 4.76 (br t, 2H), 4.33-4.21 (m, 3H), 3.88 (s, 3H), 3.45 (s, 3H), 3.38 (s, 3H), 3.16 (br t, 2H), 2.59-2.43 (m, 3H), 1.27-1.10 (m, 18H). MS (ESI) m/z: 799 $(M+1)^+$.

Example 33: Compound 33




TFA (1 mL) was added to a solution of 127 (15 mg, 0.014 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 2 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give 33 as a white solid (19 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 8.96-8.90 (m, 1H), 7.67-7.52 (m, 3H), 7.40-7.24 (m, 2H), 7.13-7.08 (m, 2H), 6.84-6.80 (m, 1H), 4.86-4.67 (m, 3H), 3.95 (s, 3H), 3.55-3.43 (m, 12H), 2.66-2.35 (m, 6H), 2.27-2.14 (m, 6H). MS (ESI) m/z: 791 $(M+1)^+$.

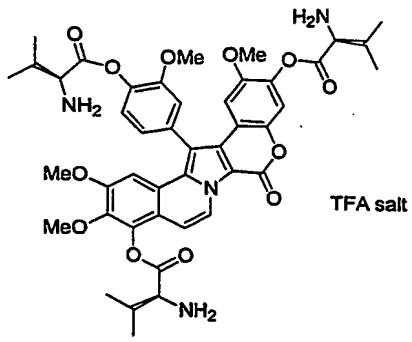
Example 34: Compound 34



A suspension of 109 (50 mg, 0.0997 mmol), Boc-D-Val-OH (87 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in anhydrous $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 3 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL). The aqueous phase was extracted with $CH_2Cl_2$ (10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 50:1) to give 34 as a white solid (100 mg, 91%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.26-7.08 (m, 4H), 6.97 (s, 1H), 6.77 (d, $J$= 7.1 Hz, 1H), 6.69 (d, $J$= 9.3 Hz, 1H), 5.07-5.05 (m, 3H), 4.96-4.90 (m, 1H), 4.75-4.70 (m, 1H), 4.55-4.47 (m, 3H), 3.78

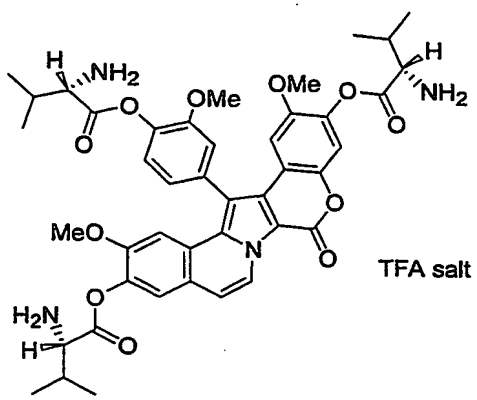
(s, 3H), 3.40 (s, 3H), 3.33 (s, 3H), 3.21 (br t, 2H), 2.45-2.30 (m, 3H), 1.49 (s, 9H), 1.47 (s, 18H), 1.12-0.99 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.5, 170.3 (2C), 155.6, 154.9, 152.0, 149.7, 147.5, 144.8, 139.6, 139.1, 138.5, 134.9, 134.2, 126.9, 125.9, 125.7, 123.8, 123.1, 122.5, 116.1, 115.8, 114.9, 114.6, 111.8, 109.6, 105.4, 79.9 (3C), 58.5, 55.9, 55.5, 55.5, 55.3, 55.2, 42.3, 31.5, 31.2, 31.1, 28.2 (9C), 27.9, 19.0 (2C), 17.1 (4C). MS (ESI) m/z: 1099 $(M+1)^+$. Rf: 0.35 ($CH_2Cl_2$:MeOH 50:1).

Example 35: Compound **35**




TFA (1 mL) was added to a solution of **129** (15 mg, 0.013 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **35** was obtained as a white solid (13 mg, 98%). The solid was collected by triturating in $Et_2O$ and filtrating. $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.14 (dd, $J$= 7.5, 3.0 Hz, 1H), 7.60-7.50 (m, 2H), 7.50-7.20 (m, 4H), 6.87 (d, $J$= 11.1 Hz, 1H), 4.60-4.50 (m, 1H), 4.40-4.30 (m, 1H), 4.25-4.20 (m, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.52 (s, 3H), 3.47 (s, 3H), 2.80-2.40 (m, 3H), 1.40-1.10 (m, 18H). MS (ESI) m/z: 827 $(M+1)^+$.

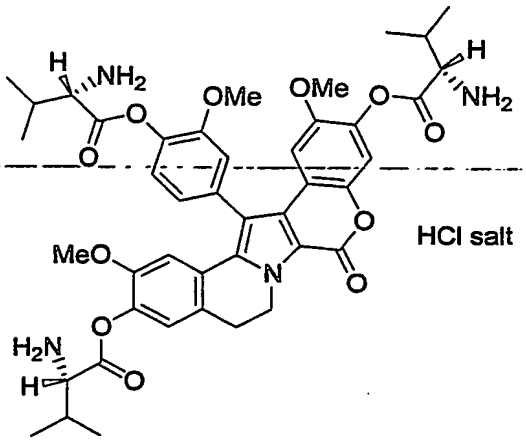
Example 36: Compound **36**




TFA (1 mL) was added to a solution of **38** (15 mg, 0.014 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 4 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **36** as a white solid (21 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.09-9.04 (m, 1H), 7.62-7.51 (m, 3H), 7.41-7.32 (m, 2H), 7.23-7.18 (m, 2H), 6.88 (d, $J$= 9.0 Hz, 1H), 4.36

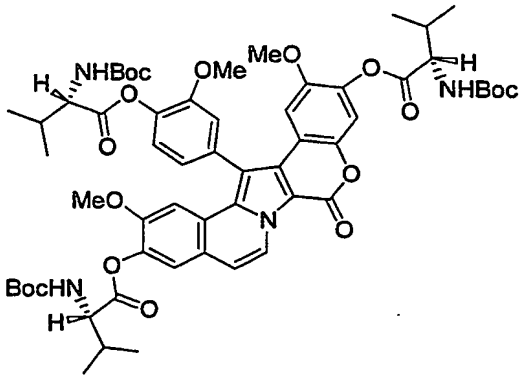
(d, $J$= 4.4 Hz, 1H), 4.31 (d, $J$= 4.4 Hz, 1H), 4.24 (t, $J$= 4.4 Hz, 1H), 3.92 (s, 3H), 3.48 (s, 6H), 2.62-2.43 (m, 3H), 1.29-1.19 (m, 18H). MS (ESI) m/z: 797 $(M+1)^+$.

Example 37: Compound **37**




$ClSiMe_3$ (10 µL, 0.079 mmol) was added at 0 °C to a solution of **144** (12 mg, 0.011 mmol) in MeOH (1 mL). The reaction mixture was stirred for 4 h at 23 °C, then $ClSiMe_3$ (5 µL, 0.395 mmol) was added and the mixture stirred at 23 °C for another 19 h. The solvent was evaporated under reduced pressure and the residue treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **37** as a white solid (7 mg, 70%). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.46-7.43 (m, 2H), 7.26-7.16 (m, 3H), 6.89-6.78 (m, 2H), 4.80 (br t, 2H), 4.33 (s, 1H), 4.24 (s, 2H), 3.84 (s, 3H), 3.45 (s, 3H), 3.37 (s, 3H), 3.18 (br t, 2H), 2.60-2.40 (m, 3H), 1.27-1.17 (m, 18H). $^{13}$C NMR (75 MHz, $CD_3OD$) $\delta$ 168.7, 168.3 (2C), 156.2, 153.5, 150.8, 148.8, 146.1, 140.6, 140.0, 139.3, 136.6, 136.4, 128.4, 128.0, 127.5, 125.2, 124.7, 123.7, 117.9, 117.6, 116.5, 116.2, 112.8, 110.9, 106.7, 59.5, 59.4, 56.9, 56.4, 56.2, 56.0, 43.7, 31.3 (3C), 28.8, 18.3 (2C), 18.2 (4C). MS (ESI) m/z: 799 $(M+1)^+$.

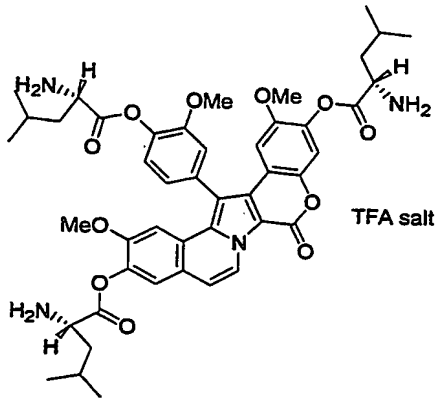
Example 38: Compound **38**




A suspension of **144** (49 mg, 0.045 mmol) and DDQ (20 mg, 0.089 mmol) in $CCl_4$ (2 mL) was refluxed for 5 h. The mixture was cooled to 23 °C then filtered through Celite and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH,

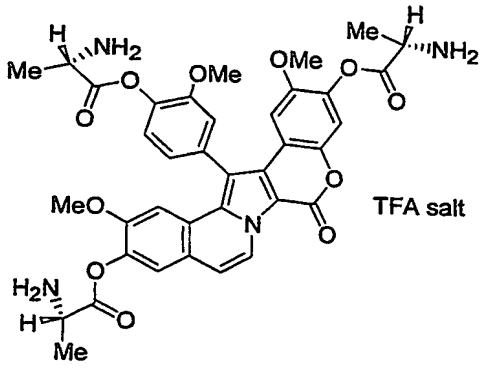
from 100:1 to 50:1) to give **38** (43 mg, 88%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.20 (d, $J$= 7.3 Hz, 1H), 7.40 (s, 1H), 7.30-7.13 (m, 5H), 7.04 (d, $J$= 7.3 Hz, 1H), 6.79 (d, $J$= 7.5 Hz, 1H), 5.10-5.06 (m, 3H), 4.56-4.48 (m, 3H), 3.81 (s, 3H), 3.43 (s, 6H), 2.45-2.32 (m, 3H), 1.49 (s, 9H), 1.47 (s, 18H), 1.14-1.00 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.4 (3C), 155.7, 155.0, 152.3, 150.9, 147.6, 145.4, 140.6, 140.0, 139.4, 134.5, 133.5, 130.9, 128.8, 128.2, 128.1, 124.1, 123.8, 123.6, 123.2, 120.8, 115.9, 115.1, 112.8, 112.3, 112.2, 109.1, 106.4, 106.2, 80.0 (3C), 58.5, 56.0, 55.6, 55.6, 55.5, 55.5, 31.3 (2C), 31.2, 28.3 (9C), 19.2, 19.1, 17.2 (2C), 17.1 (2C). MS (ESI) m/z: 1119 $(M+23)^+$, 1097 $(M+1)^+$. Rf: 0.33 ($CH_2Cl_2$:MeOH, 100:1).

Example 39: Compound **39**




TFA (1 mL) was added to a solution of **146** (15 mg, 0.013 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 5 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **39** as a white solid (19 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.15-9.12 (m, 1H), 7.64 (d, $J$= 2.7 Hz, 1H), 7.58-7.52 (m, 2H), 7.40-7.29 (m, 2H), 7.26-7.22 (m, 2H), 6.89 (d, $J$= 7.3 Hz, 1H), 4.45-4.31 (m, 3H), 3.90 (s, 3H), 3.48 (s, 3H), 3.48 (s, 3H), 2.11-1.79 (m, 9H), 1.13-1.06 (m, 18H). MS (ESI) m/z: 839 $(M+1)^+$.

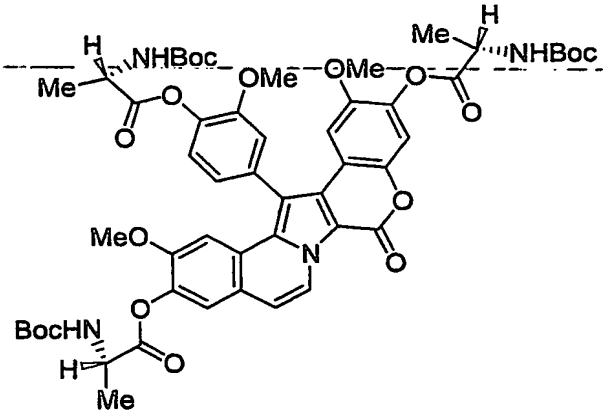
Example 40: Compound **40**




TFA (1 mL) was added to a solution of **41** (15 mg, 0.015 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 5 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining

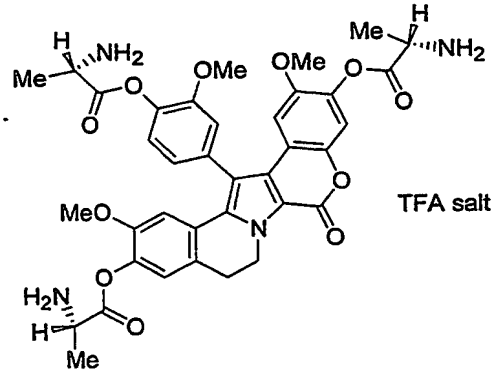
TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **40** as a white solid (16 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.03-8.99 (m, 1H), 7.63-7.60 (m, 2H), 7.52 (dd, $J$= 8.0, 1.6 Hz, 1H), 7.39-7.27 (m, 2H), 7.18-7.15 (m, 2H), 6.85 (d, $J$=9.2 Hz, 1H), 4.53-4.36 (m, 3H), 3.93 (s, 3H), 3.48 (s, 6H), 1.80 (d, $J$= 7.1 Hz, 3H), 1.74 (d, $J$= 7.3 Hz, 3H), 1.71-1.68 (m, 3H). MS (ESI) m/z: 713 $(M+1)^+$.

Example 41: Compound **41**




A suspension of **156** (63 mg, 0.062 mmol) and DDQ (21 mg, 0.093 mmol) in $CHCl_3$ (5 mL) was refluxed for 2 days. The mixture was cooled at 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give **41** (58 mg, 92%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.24 (d, $J$= 7.3 Hz, 1H), 7.44-7.32 (m, 2H), 7.25-7.18 (m, 4H), 7.07 (d, $J$= 7.5 Hz, 1H), 6.79 (d, $J$= 7.5 Hz, 1H), 5.11-5.09 (m, 3H), 4.64-4.60 (m, 3H), 3.81 (s, 3H), 3.44 (s, 6H), 1.63-1.55 (m, 9H), 1.49 (s, 9H), 1.47 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.5, 171.3, 171.1, 155.0, 154.8, 152.2, 150.8, 147.6, 145.3, 140.6, 140.0, 139.4, 134.4, 133.3, 128.0, 127.9, 123.9, 123.7, 123.7, 123.7, 123.6, 123.0, 120.6, 115.7, 115.1, 112.7, 112.2, 112.0, 108.9, 106.3, 106.1, 80.0 (3C), 56.2 (2C), 55.8, 55.7, 55.7, 55.5, 28.3 (9C), 18.6 (3C). MS (ESI) m/z: 1035 $(M+23)^+$, 1013 $(M+1)^+$. Rf: 0.43 (hexane:EtOAc, 50:50).

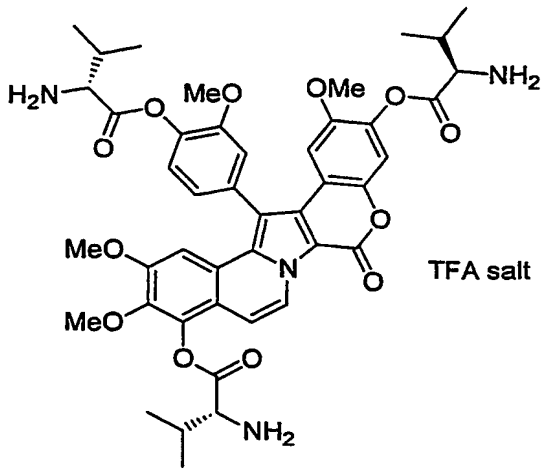
Example 42: Compound **42**




TFA (1 mL) was added to a solution of **156** (15 mg, 0.0148 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 2 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining

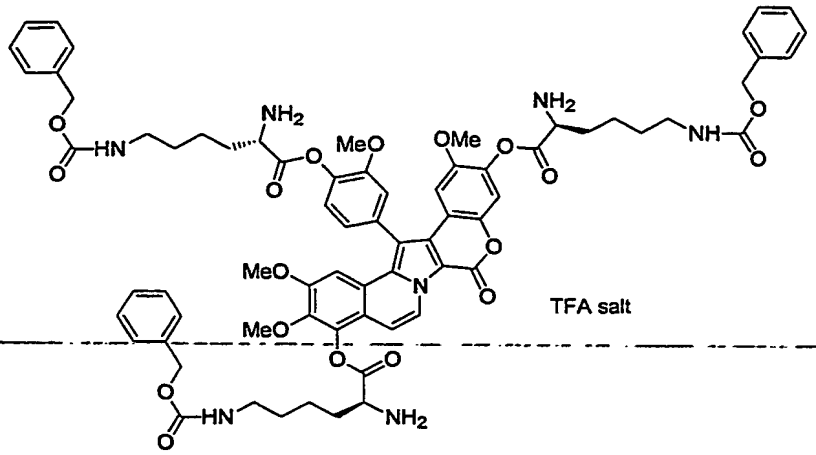
TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **42** as a white solid (17 mg, quant.) $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.46-7.44 (m, 2H), 7.28-7.27 (m, 1H), 7.19 (s, 1H), 7.16 (s, 1H), 6.87 (d, $J$= 8.8 Hz, 1H), 6.78 (d, $J$= 10.0 Hz, 1H), 4.75 (t, $J$= 6.2 Hz, 2H), 4.77-4.37 (m, 3H), 3.87 (s, 3H), 3.45 (s, 3H), 3.38 (s, 3H), 3.16 (t, $J$= 6.2 Hz, 2H), 1.77 (d, $J$= 6.9 Hz, 3H), 1.71-1.67 (m, 6H). MS (ESI) m/z: 715 $(M+1)^+$.

Example 43: Compound **43**



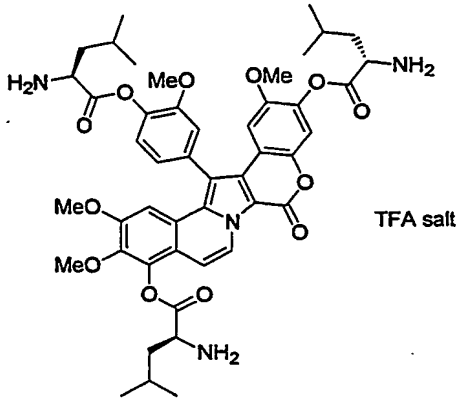

TFA (1 mL) was added to a solution of **160** (13.0 mg, 0.0115 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 45 min. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x5 mL) and evaporated to dryness to give **43** as a white solid (13.0 mg, quant.) $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.18 (d, $J$= 7.6 Hz, 1H), 7.56-7.52 (m, 2H), 7.40-7.22 (m, 4H), 6.90 (d, $J$= 10.7 Hz, 1H), 4.60-4.59 (m, 1H), 4.37-4.35 (m, 1H), 4.26-4.24 (m, 1H), 3.90 (br s, 6H), 3.54 (br s, 3H), 3.47 (s, 3H); 2.62-2.47 (s, 3H), 1.32-1.19 (s, 18H). $^{13}$C NMR (75 MHz, $CD_3OD$) $\delta$ 168.8 (2C), 168.2, 154.6, 153.8, 148.9, 146.6, 143.1, 141.0, 140.2, 139.1, 136.4, 134.5 (2C), 129.5 (2C), 125.3, 125.1, 124.5, 122.1, 119.1, 116.8, 113.9, 113.1, 110.2, 107.7, 107.4, 106.0, 61.4, 59.5 (3C), 56.9, 56.2 (2C), 31.3 (3C), 18.5, 18.3, 18.2 (2C), 18.1, 17.9. MS (ESI) m/z: 827 $(M+1)^+$.

Example 44: Compound **44**



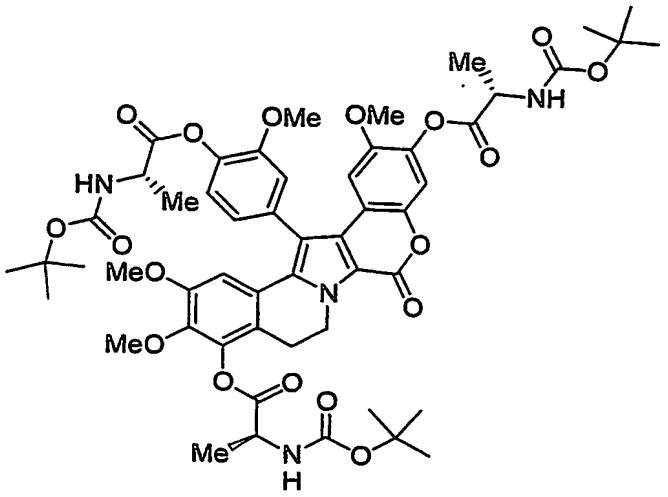

TFA (1 mL) was added to a solution of **158** (11.4 mg, 0.0070 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 45 min. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x5 mL) and evaporated to dryness to give **44** as a yellow solid (12.3 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.20 (d, $J$= 8.1 Hz, 1H); 7.55-7.47 (m, 2H), 7.27-7.18 (m, 19H), 6.87 (d, $J$= 9.3 Hz, 1H), 5.03 (s, 6H), 4.65 (br t, 1H), 4.49 (br t, 1H), 4.36 (br t, 1H), 3.88 (br s, 3H), 3.85 (br s, 3H), 3.51 (br s, 3H), 3.46 (br s, 3H), 3.22-3.18 (m, 6H), 2.40-2.00 (m, 6H), 1.65-1.50 (m, 12H). MS (ESI) m/z: 1339 $(M+23)^+$, 1316 $(M+1)^+$.

Example 45: Compound **45**



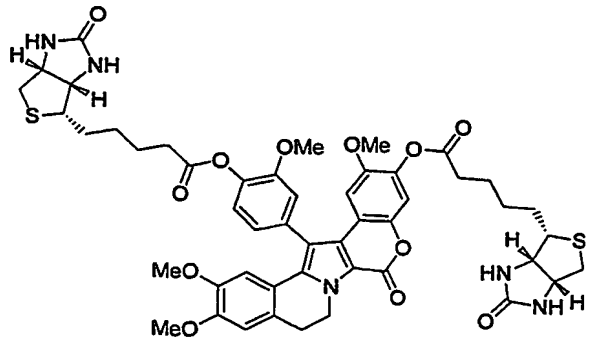

TFA (1 mL) was added to a solution of **159** (21.1 mg, 0.018 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 45 min. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x5 mL) and evaporated to dryness to give **45** as a white solid (27.3 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 9.20 (d, $J$= 7.6 Hz, 1H), 7.56-7.51 (m, 2H), 7.40-7.22 (m, 4H), 6.89 (d, $J$= 8.3 Hz, 1H), 4.64 (t, $J$= 6.0 Hz, 1H), 4.44 (t, $J$= 6.3 Hz, 1H), 4.34 (t, $J$= 7.2 Hz, 1H), 3.89 (br s, 6H), 3.54 (br s, 3H), 3.48 (br s, 3H), 2.19-1.79 (m, 9H), 1.15-1.07 (m, 18H). MS (ESI) m/z: 869 $(M+1)^+$.

Example 46: Compound **46**



A suspension of 1 (50 mg, 0.0494 mmol), (L)-N-Boc-Alanine (107 mg, 0.56 mmol), EDC·HCl (108 mg, 0.56 mmol) and DMAP (7.0 mg, 0.056 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 3 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with $H_2O$ (20 mL) and saturated aqueous solution of $NaHCO_3$ (20 mL), dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give 46 as a yellow solid (80 mg, 80%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.28-7.20 (m, 1H), 7.20-7.05 (m, 3H), 6.67 (d, $J$= 3.7 Hz, 1H), 6.65 (d, $J$= 4.0 Hz, 1H), 5.15-5.05 (m, 2H), 4.70-4.50 (m, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.40 (s, 3H), 3.38 (s, 3H), 3.01 (br t, 2H), 1.70-1.50 (m, 9H), 1.48 (s, 9H), 1.47 (s, 9H), 1.46 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.8, 171.4, 155.0, 152.1, 151.8, 147.5, 144.9, 144.8, 141.3, 141.0, 139.8, 138.7, 134.8, 134.7, 134.3, 127.1, 127.0, 123.7, 123.2, 122.7, 119.7, 119.4, 116.2, 115.7, 114.9, 114.7, 111.8, 107.6, 105.5, 80.2, 80.1 (2C), 60.8, 56.2, 55.7, 55.5, 49.5, 49.3 (2C), 41.9, 28.3 (9C), 22.1, 18.7, 18.6, 18.3. MS (ESI) m/z: 1067.3 $(M+23)^+$, 1045 $(M+1)^+$. Rf: 0.70 (hexane:EtOAc 1:2).

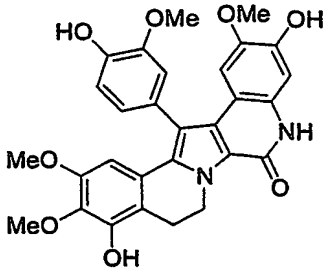
Example 47: Compound 47



A suspension of (+)-Biotine (59 mg, 0.56 mmol) , EDC·HCl (46 mg, 0.242 mmol) and DIPEA (0.17 mL, 0.96 mmol) in $CH_2Cl_2$ (2 mL) was stirred at 23 °C for 5 minutes, then 95 (25 mg, 0.048 mmol) was added and the mixture stirred at 23 °C for 24 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL) and washed with HCl 0.1 N (2x20 mL), the aqueous phase was extracted with $CH_2Cl_2$ (3x50 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and

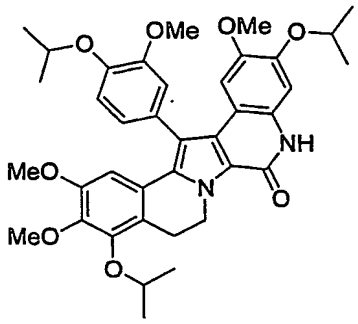
evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 10:1) to give 47 as a white solid (5 mg, 10%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.30-7.10 (m, 4H), 6.80-6.60 (m, 3H), 6.40 (br s, 1H), 6.30 (br s, 1H), 6.20 (br s, 1H), 6.10 (br s, 1H), 4.90-4.70 (m, 2H), 4.60-4.45 (m, 2H), 4.40-4.25 (m, 2H), 3.90 (s, 3H), 3.80 (s, 3H), 3.45 (s, 3H), 3.39 (s, 3H), 3.20-3.10 (m, 4H), 3.00-2.50 (m, 8H), 2.00-1.50 (m, 12H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.6, 171.3, 163.8, 155.2, 152.1, 149.1, 147.6, 144.9, 139.8, 139.0, 135.7, 134.2, 127.4, 126.5, 123.8, 123.5, 123.3, 119.7, 116.0, 114.8, 114.4, 111.8, 111.0, 108.5, 105.4, 62.3, 62.2, 61.4, 60.3, 59.9, 56.2, 56.1, 55.9, 55.8, 55.5, 55.3, 55.2, 42.5, 40.6, 40.5, 33.8, 33.1, 29.7, 28.6, 28.2, 28.1, 27.8, 27.4, 25.1, 24.7, 21.0, 14.2. MS (ESI) m/z: 990 $(M+23)^+$, 968 $(M)^+$. Rf: 0.20 ($CH_2Cl_2$:MeOH, 10:1).

Example 48: Compound 48




A suspension of 49 (15.0 mg, 0.022 mmol) and $AlCl_3$ (18.3 mg, 0.137mmol) in anhydrous $CH_2Cl_2$ (2 mL) was stirred from 0 °C to 23 °C for 2 h under Argon atmosphere. MeOH (1 mL) was added and the solvent was evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 10:1) to provide 48 as a beige solid (9.9 mg, 84%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.60 (br s, 1H), 7.15-7.07 (m, 2 H), 7.00 (br s, 1H), 6.82 (s, 1H), 6.72 (s, 1H), 6.40 (s, 1H), 6.02 (br s, 1H), 5.80 (br s, 2H), 5.16-5.08 (m, 1H), 4.85-4.78 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.47 (s, 3H), 3.36 (s, 3H), 3.18-3.10 (m, 2H). MS (ESI) m/z: 531 $(M+1)^+$. Rf: 0.25 ($CH_2Cl_2$:MeOH, 10:1).

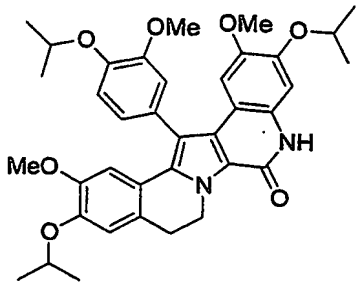
Example 49: Compound 49




8-isopropoxy-6,7-dimethoxy-3,4-dihydroisoquinoline (100 mg, 0.401 mmol) was added to a solution of LL-10-amide (195.9 mg, 0.365 mmol) in dry dimethylacetamide (5 mL) under Argon atmosphere. The solution was stirred at 23 °C for 24 h, then $Et_3N$ (50 µL, 0.365 mmol) was added and the reaction mixture was heated at 80 °C for 18 h. The solution was cooled to 23 °C, then $(KSO_3)_2NO$ (97.8 mg, 0.365 mmol) and saturated

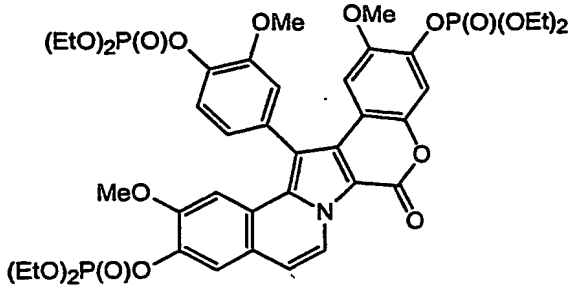
aqueous solution of $Na_2CO_3$ (1 mL) were added and the suspension was stirred for 1 h at 23 °C. After this time, the mixture was treated with saturated aqueous solution of $NaHCO_3$ and extracted with $CH_2Cl_2$. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and the solvent was evaporated under reduced pressure. The resulted residue was purified by chromatography on silica gel (EtOAc:hexane, 4:1) to provide 49 as a beige solid (55.7 mg, 21%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.10-7.08 (m, 3H), 7.00 (s, 1H), 6.77 (s,1H), 6.63 (s, 1H), 4.99 (br t, 2H), 4.63-4.53 (m, 3H), 3.83 (s, 6H), 3.41 (s, 3H), 3.35 (s, 3H), 3.16 (br t, 2H), 1.42 (d, $J$= 5.4 Hz, 6H), 1.40 (d, 5.4 Hz, 6H), 1.32 (d, 6.1 Hz, 6H). %). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 156.7, 151.7, 151.3, 148.5, 146.8, 145.9, 142.0, 133.3, 129.8, 129.7, 127.3, 123.7, 123.6, 121.0, 118.9, 117.0, 115.4, 114.9, 111.2, 105.3, 104.9, 102.6, 75.7, 71.8, 71.6, 60.5, 56.2, 55.3, 55.1, 42.3, 23.0, 22.7 (2C), 22.0 (2C), 21.9 (2C). MS (ESI) m/z: 657 $(M+1)^+$. Rf: 0.34 (EtOAc:hexane, 4:1).

Example 50: Compound 50



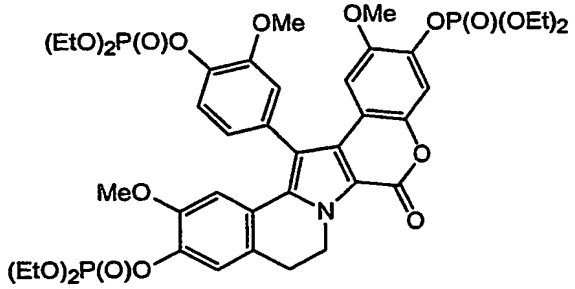

6-isopropoxy-7-methoxy-3,4-dihydroisoquinoline (100 mg, 0.456 mmol) was added to a solution of LL-10-amide (222.8 mg, 0.4146 mmol) in dry dimethylacetamide (5 mL) under Argon atmosphere. The solution was stirred at 23 °C for 24 h, then $Et_3N$ (58 µL, 0.414 mmol) was added and the reaction mixture was heated at 80 °C for 18 h. The solution was cooled to 23 °C, then $(KSO_3)_2NO$ (111.2 mg, 0.414 mmol) and saturated aqueous solution of $Na_2CO_3$ (1 mL) was added and the suspension was stirred for 1 h at 23 °C. After this time, the mixture was treated with saturated aqueous solution of $NaHCO_3$ and extracted with $CH_2Cl_2$. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and the solvent was evaporated under reduced pressure. The resulted residue was purified by chromatography on silica gel (EtOAc) to provide 50 as a white solid (51.7 mg, 18%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.09-7.08 (m, 3H), 6.95 (br s, 1H), 6.80-6.76 (m, 3H), 5.03-5.00 (m, 2H), 4.62-4.52 (m, 3H), 3.81 (s, 3H), 3.41 (s, 3H), 3.34 (s, 3H), 3.11 (t, $J$= 6.3 Hz, 2H), 1.42-1.34 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 156.1, 151.1, 148.4, 146.5, 145.8, 134.0, 129.6, 129.3, 127.4, 126.3, 123.5, 120.7, 118.4, 116.9, 114.7, 114.4, 111.1, 109.0, 105.0, 102.3, 71.8, 71.4, 71.3, 55.9, 55.0, 54.9, 42.3, 28.7, 21.7 (6C). MS (ESI) m/z: 627 $(M+1)^+$. Rf: 0.42 (EtOAc).

Example 51: Compound 51




A suspension of **52** (11 mg, 0.012 mmol) and DDQ (6 mg, 0.024 mmol) in $CHCl_3$ (2 mL) was refluxed for 21 h. The mixture was cooled to 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to give **51** (7 mg, 64%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.24 (d, $J$= 7.3 Hz, 1H), 7.63 (d, $J$= 1.2 Hz, 1H), 7.53 (dd, $J$= 8.0, 1.7 Hz, 1H), 7.37 (d, $J$= 1.5 Hz, 1H), 7.23-7.15 (m, 3H), 7.08 (d, $J$= 7.3 Hz, 1H), 6.76 (s, 1H), 4.38-4.22 (m, 12H), 3.88 (s, 3H), 3.48 (s, 3H), 3.47 (s, 3H), 1.45 (t, $J$= 7.0 Hz, 6H), 1.38 (t, $J$= 7.0 Hz, 12H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.1, 152.0 (d, $J_{C\text{-}P}$= 4.5 Hz), 150.6 (d, $J_{C\text{-}P}$= 5.5 Hz), 147.4 (d, $J_{C\text{-}P}$= 5.0 Hz), 145.5, 140.9 (d, $J_{C\text{-}P}$= 7.1 Hz), 140.2 (d, $J_{C\text{-}P}$= 7.1 Hz), 139.9 (d, $J_{C\text{-}P}$= 7.1 Hz), 133.5, 133.3, 128.2, 123.9, 123.7, 123.3, 122.8 (d, $J_{C\text{-}P}$= 3.0 Hz), 122.6, 118.8, 115.4, 114.6, 112.8, 111.9, 110.8, 108.9, 106.5, 106.3, 64.9, 64.8 (2C), 64.7 (2C), 64.6, 56.3, 55.8, 55.6, 16.2, 16.1 (3C), 16.0. MS (ESI) m/z: 908 $(M+1)^+$. Rf: 0.29 ($CH_2Cl_2$:MeOH, 20:1).

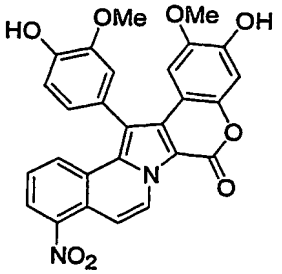
Example 52: Compound **52**




To a suspension of **109** (15 mg, 0.030 mmol) in $CH_2Cl_2$ under Argon atmosphere, triethylamine (17 µL, 0.120 mmol) and diethyl chlorophosphate (18 µL, 0.120 mmol) were added and the mixture stirred at 23 °C. After 4.5 h, two more equivalents of triethylamine (9 µL, 0.060 mmol) and diethyl chlorophosphate (9 µL, 0.060 mmol) were added and the mixture stirred at 23 °C overnight. The mixture was concentrated under reduced pressure and the residue purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 30:1 to 15:1) to give **52** as a white solid (20 mg, 74%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.45 (dd, $J$= 8.1, 1.5 Hz, 1H), 7.29 (d, $J$=1.5 Hz, 1H), 7.18 (s, 1H), 7.10 (dd, $J$= 8.1, 1.6 Hz, 1H), 7.06 (s, 1H), 6.71 (s, 1H), 6.64 (s, 1H), 4.94-4.86 (m, 1H), 4.72-4.63 (m, 1H), 4.34-4.18 (m, 12H), 3.84 (s, 3H), 3.44 (s, 3H), 3.36 (s, 3H), 3.09 (br t, 2H), 1.44-1.31 (m, 18H). %). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.1, 151.7 (d, $J_{C\text{-}P}$= 4.5 Hz), 149.3 (d, $J_{C\text{-}P}$= 5.5 Hz), 147.4 (d, $J_{C\text{-}P}$= 5.0 Hz), 144.9, 139.9 (d, $J_{C\text{-}P}$= 7.1 Hz), 139.6 (d, $J_{C\text{-}P}$= 6.5 Hz), 139.1 (d, $J_{C\text{-}P}$= 7.6 Hz), 135.0, 133.0, 127.0, 126.2, 124.4, 123.2, 122.6, 122.6, 121.1, 115.5, 114.9, 114.8, 110.5, 109.8, 105.6, 64.7, 64.7, 64.7

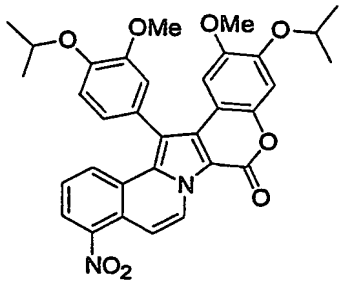
(3C), 64.6, 56.2, 55.8, 55.5, 42.4, 28.1, 16.2, 16.1 (3C), 16.0, 16.0. MS (ESI) m/z: 910 $(M+1)^+$. Rf: 0.23 ($CH_2Cl_2$:MeOH, 30:1).

Example 53: Compound 53



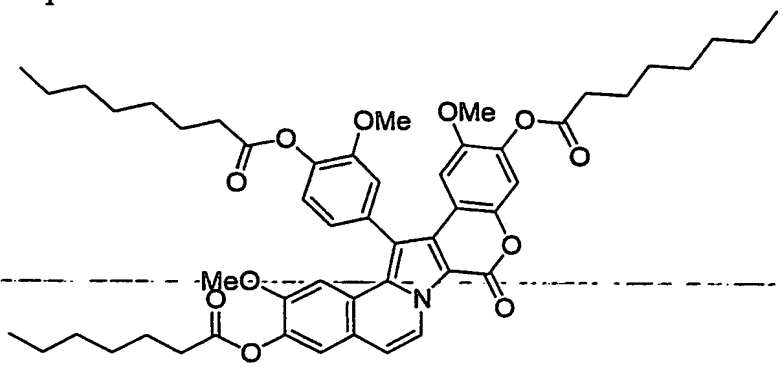

Aluminium chloride (110 mg, 0.82 mmol) was added to a solution of 54 (160 mg, 0.27 mmol) in anhydrous $CH_2Cl_2$ (5 mL) under Argon atmosphere. The reaction mixture was stirred for 1 h at 23 °C. The mixture was quenched with $CH_2Cl_2$:MeOH (20:1, 20 mL), silica gel (8.0 g) was added and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel ($CH_2Cl_2$:MeOH, from 20:1 to 10:1) to provide 53 as a yellow solid (70 mg, 51%). $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.30 (d, $J$= 7.6 Hz, 1H), 8.20 (d, $J$= 7.7 Hz, 1H), 8.08 (d, $J$= 8.0 Hz, 1H), 7.70-7.50 (m, 2H), 7.20-7.10 (m, 2H), 7.00 (d, $J$= 7.8 Hz, 1H), 6.88 (s, 1H), 6.57 (s, 1H), 5.69 (s, 1H), 3.76 (s, 3H), 3.40 (s, 3H). MS (ESI) m/z: 499 $(M+1)^+$. Rf: 0.61 ($CH_2Cl_2$:MeOH, 10:1).

Example 54: Compound 54



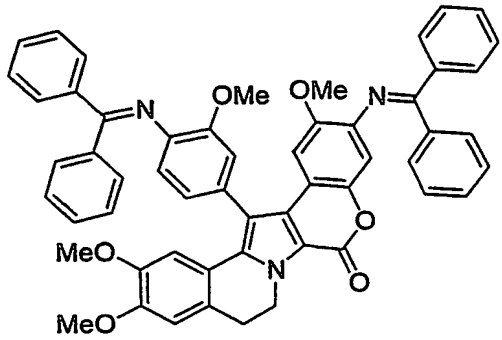

LL-10-Br (491 mg, 1.0 mmol) was added in one portion to a solution of 5-nitroisoquinoline (199 mg, 1.12 mmol) in dry 1,2-dichloroethane (10 mL) under Argon atmosphere. The solution was stirred at 23 °C for 16 h, then diisopropylethylamine (0.38 mL) was added and the reaction mixture was heated at 85 °C for 64 h. The reaction mixture was cooled to 23 °C, silica gel (1.5 g) was added and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel (hexane:$CH_2Cl_2$:$Et_2O$, from 5:5:1 to 5:5:2) to provide 54 as a yellow solid (190 mg, 33%). $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 9.41 (d, $J$= 7.8 Hz, 1H), 8.12 (dd, $J$= 7.8, 1.1 Hz, 1H), 8.06 (dt, $J$= 8.0, 0.9 Hz, 1H), 7.78 (dd, $J$= 7.8, 0.7 Hz, 1H), 7.36 (t, $J$= 8.2 Hz, 1H), 7.19 (d, $J$= 8.2 Hz, 1H), 7.11 (dd, $J$= 8.2, 1.8 Hz, 1H), 7.05 (d, $J$= 1.8 Hz, 1H), 6.96 (s, 1H), 6.63 (s, 1H), 4.71 (hp, $J$= 6.0 Hz, 1H), 4.58 (hp, $J$= 6.0 Hz, 1H), 3.84 (s, 3H), 3.44 (s, 3H), 1.51 (d, $J$= 6.0 Hz, 3H), 1.44 (d, $J$= 6.0 Hz, 3H), 1.40 (d, $J$= 7.8 Hz, 6H). MS (ESI) m/z: 583 $(M+1)^+$. Rf: 0.50 (hexane:$CH_2Cl_2$:$Et_2O$, 5:5:2).

Example 55: Compound **55**




A suspension of **28** (16 mg, 0.018 mmol) and DDQ (9 mg, 0.036 mmol) in $CHCl_3$ (2 mL) was refluxed for 15 h. The mixture was cooled to 23 °C then filtered through Celite and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 100:1) to give **55** (17 mg, quantitative). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$= 7.5 Hz, 1H), 7.38 (s, 1H), 7.30-7.13 (m, 5H), 7.05 (d, $J$= 7.3 Hz, 1H), 6.81 (s, 1H), 3.82 (s, 3H), 3.45 (s, 6H), 2.65-2.55 (m, 6H), 1.82-1.73 (m, 6H), 1.42-1.25 (m, 24H), 0.91-0.85 (m, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.7, 171.6, 171.6, 155.1, 152.4, 151.1, 147.8, 145.5, 141.0, 140.4, 139.9, 134.1, 133.6, 128.3, 124.1, 123.8, 123.6, 123.6, 123.1, 120.7, 115.6, 115.0, 112.8, 112.3, 112.2, 109.0, 106.4, 106.1, 56.2, 55.8, 55.6, 34.0 (3C), 31.7 (3C), 29.7, 29.0 (2C), 28.9 (3C), 25.0, 25.0, 24.9, 22.6 (3C), 14.1 (3C). MS (ESI) m/z: 878 $(M+1)^+$. Rf: 0.31 ($CH_2Cl_2$:MeOH, 100:1).

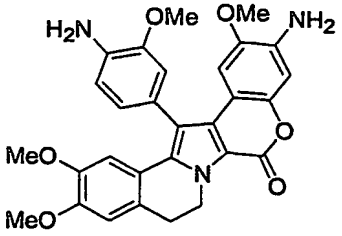
Example 56: Compound **56**




A suspension of **86** (0.2248 g, 0.288 mmol), $Pd(OAc)_2$ (3.8 mg, 0.017 mmol), BINAP (16.2 mg, 0.026 mmol), and $Cs_2CO_3$ (0.263 g, 0.807 mmol) in anhydrous Toluene (5 mL) was stirred at 23 °C under Argon atmsphere for 5 min. Then benzophenone imine (116 mL, 0.692 mmol) was added and the mixture was heated at 110 °C for 3 d. The reaction was cooled to 23 °C, $CH_2Cl_2$ was added (20 mL), and washed with $H_2O$ (20 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and evaporated to dryness. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give LL-MA-triflate-$NPh_2$ (56.2 mg, 24%) and **56** (0.102 g, 42%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.76-7.70 (m, 4H), 7.48-7.37 (m, 7H), 7.32-7.20 (m, 7H), 7.14-7.10 (m, 2H), 6.98 (dd, $J$= 7.8 ,1.5 Hz, 1H), 6.91 (d, $J$=1.5 Hz, 1H), 6.77 (d, $J$= 7.8 Hz, 1H), 6.74 (s, 1H), 6.71 (s, 1H), 6.60 (s, 1H), 6.59 (s, 1H), 4.89-4.81 (m, 1H), 4.68-4.59

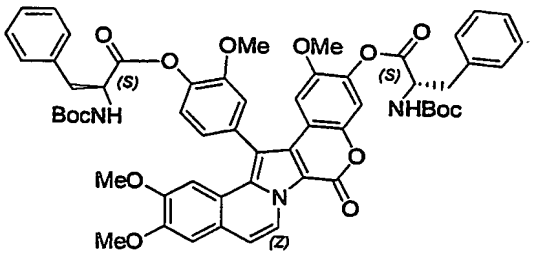
(m, 1H), 3.90 (s, 3H), 3.68 (s, 3H), 3.35 (s, 3H), 3.27 (s, 3H), 3.05 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.2, 169.2, 155.4, 150.1,148.8, 147.4, 146.3, 145.4, 140.9, 140.7, 139.3, 138.9, 136.8, 136.3, 135.6, 130.8, 130.7, 130.6, 129.4, 129.3, 128.7, 128.6, 128.5, 128.4, 128.0, 127.7, 127.6, 126.6, 123.3, 120.9, 119.9, 115.1, 114.0, 113.9, 113.4, 110.8, 109.0, 108.9, 104.6, 558, 55.6, 55.5, 55.4, 42.2, 28.6. MS (ESI) m/z: 842 $(M+1)^+$. Rf: 0.33 (hexane:EtOAc, 50:50).

Example 57: Compound **57**




HCl 1.5 N (1.5 mL) was added to a solution of **56** (91.0 mg, 0.108 mmol) in THF (20 mL) at 23 °C. The solution turned from yellow to colorless in 10 min. The solvent was evaporated to dryness and $H_2O$ was added (20 mL). The suspension was basified with aqueous ammonia (0.5 mL) and extracted with $CH_2Cl_2$ (3x20 mL), dried over anhydrous $Na_2SO_4$, filtered, and the solvent was evaporated to give a residue which was purified by chromatography on silica gel (hexane:EtOAc, 1:4) to give **57** as a white solid (55 mg, quant). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.95-6.85 (m, 3 H), 6.78 (s, 1H), 6.72 (s, 1H), 6.69 (s, 1H), 6.64 (s, 1H), 4.84-4.78 (m, 1H), 4.71-4.65 (m, 1H), 3.98 (br s, 4 H), 3.86 (s, 3H), 3.79 (s, 3H), 3.45 (s, 3H), 3.38 (s, 3H), 3.08 (br t, $J$= 7.3 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.8, 148.6, 147.7, 147.2, 146.6, 143.7, 136.4, 135.8, 135.7, 128.9, 126.4, 124.9, 123.7, 120.3, 115.0, 113.1, 112.9, 110.8, 108.7, 108.3, 103.9, 102.1, 55.8, 55.6, 55.1 (2C), 42.2, 29.2, 28.6. MS (ESI) m/z: 514 $(M+1)^+$. Rf: 0.32 (hexane:EtOAc, 1:4).

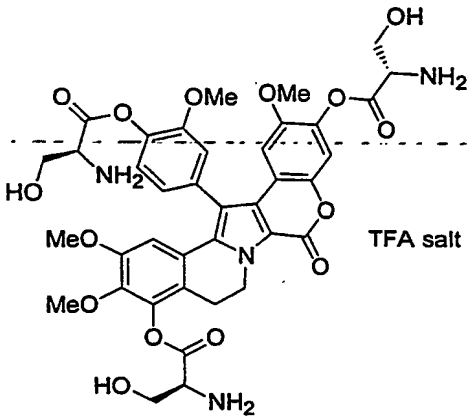
Example 58: Compound **58**




A suspension of **84** (32.2 mg, 0.0318 mmol) and DDQ (10.8 mg, 0.0478 mmol) in $CHCl_3$ (2 mL) was heated at 65 °C for 20 h under Argon atmosphere. The reaction mixture was filtered throught Celite, and washed with $CH_2Cl_2$ (50 mL), and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give **58** as a white solid (30.7 mg, 96%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.3 Hz, 1H), 7.39-7.25 (m, 11H), 7.10-7.05 (m, 6H), 6.82 (d, $J$= 7.3 Hz, 1H), 5.03 (m, 2H), 4.91 (m, 2H), 3.99 (s, 3H), 3.84 (s, 3H), 3.49 (s, 3H), 3.44 (s, 3H), 3.37-3.23 (m, 4H), 1.45 (s, 9H), 1.42 (s, 9H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.0, 154.9, 152.1, 150.3, 149.5, 147.5, 145.4, 139.8, 139.2, 135.7 (2C), 134.8, 134.2 (2C),

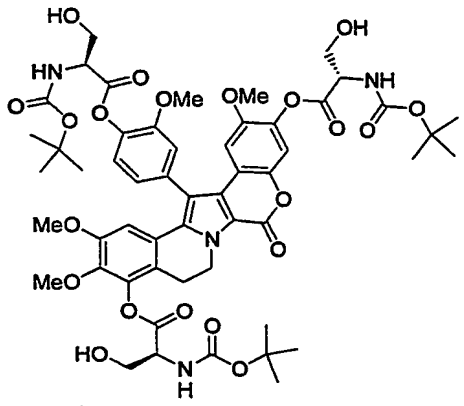
129.5, 128.6, 128.1 (2C), 124.7, 123.8, 123.0, 119.0, 16.03, 115.4, 113.0, 112.0, 110.8, 108.4, 107.4, 106.2, 105.1, 80.1 (2C), 56.1, 55.9, 55.6 (2C), 54.4 (2C), 38.1 (2C), 28.2 (6C). MS (ESI) m/z: 1008 $(M+1)^+$. Rf: 0.60 ($CH_2Cl_2$:MeOH, 60:1).

Example 59: Compound **59**




TFA (1 mL) was added to a solution of **60** (15 mg, 0.013 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **59** was obtained as a white solid (15 mg, quant.). The solid was collected by triturating in ethyl ether and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.50-7.35 (m, 2H), 7.30-7.20 (m, 2H), 6.85-6.75 (m, 2H), 4.80-4.65 (m, 2H), 4.60 (br s, 1H), 4.53 (t, $J$= 3.8 Hz, 1H), 4.42 (br t, 1H), 4.30-4.05 (m, 6H), 3.87 (s, 3H), 3.79 (s, 3H), 3.43 (s, 3H), 3.42 (s, 3H), 3.06 (br s, 2H). MS (ESI) m/z: 793 $(M+1)^+$.

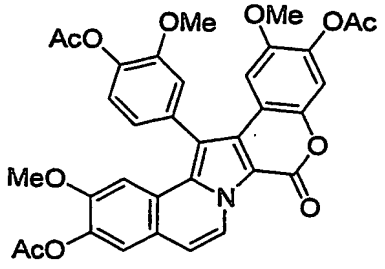
Example 60: Compound **60**




A suspension of **68** (35 mg, 0.025 mmol), Pd/C (14 mg, 10% weight) in MeOH (1 mL) was purged three times successively with Argon/Vacuum. The mixture was stirred under $H_2$ atmosphere at 23 °C overnight at 1 atm. The reaction mixture was diluted with MeOH (5 mL), filtered over Celite, washed with MeOH:EtOAc (75 mL) and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 10:1) to give **60** as a white solid (23 mg, 82%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.40-7.00 (m, 4H), 6.75-6.60 (m, 2H), 5.70-5.40 (m, 3H), 4.90-4.50 (m, 4H),

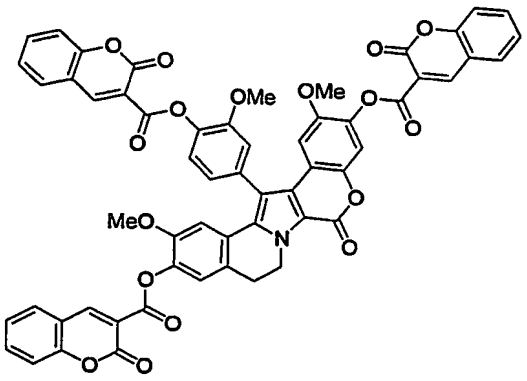
4.30-4.20 (m, 2H), 4.10-3.80 (m, 11H), 3.43 (s, 3H), 3.38 (s, 3H), 3.00 (br s, 2H), 1.49 (s, 9H), 1.48 (s, 9H), 1.46 (s, 9H). MS (ESI) m/z: 1115 $(M+23)^+$, 1093 $(M+1)^+$. Rf: 0.45 ($CH_2Cl_2$:MeOH, 10:1).

Example 61: Compound **61**




A suspension of **108** (20 mg, 0.032 mmol) and DDQ (15 mg, 0.064 mmol) in $CHCl_3$ (2 mL) was refluxed for 24 h. The mixture was cooled to 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 40:1) to give **61** (12 mg, 60%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.3 Hz, 1H), 7.39 (s, 1H), 7.30 (d, $J$= 7.7 Hz, 1H), 7.25-7.22 (m, 3H), 7.14 (s, 1H), 7.05 (d, $J$= 7.5 Hz, 1H), 6.81 (s, 1H), 3.84 (s, 3H), 3.45 (s, 6H), 2.37 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 168.9, 168.7, 168.7, 155.0, 152.4, 151.0, 147.8, 145.4, 140.9, 140.3, 139.7, 134.2, 133.5, 128.2, 124.1, 123.8, 123.7, 123.6, 123.1, 120.7, 115.7, 115.0, 112.8, 112.3, 112.2, 109.1, 106.4, 106.1, 56.2, 55.7, 55.6, 20.6 (3C). MS (ESI) m/z: 626 $(M+1)^+$. Rf: 0.40 ($CH_2Cl_2$:MeOH, 100:1).

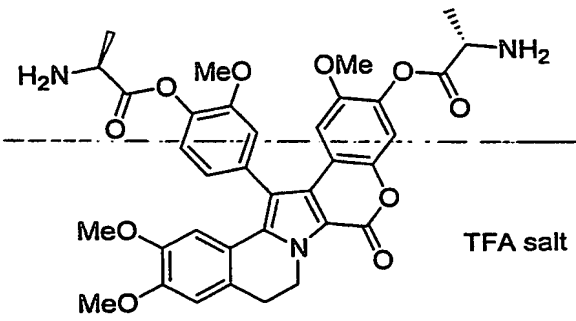
Example 62: Compound **62**




A suspension of **109** (25 mg, 0.050 mmol), coumarin 3-carboxylic acid (38 mg, 0.200 mmol), EDC·HCl (38 mg, 0.200 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$ (4.3 mL) was stirred under argon atmosphere at 23 °C for 3.5 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL). Both aqueous phases were extracted with $CH_2Cl_2$ (10 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 40:1) to give **62** as a white solid (41 mg, 80%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.80 (s, 1H), 8.79 (s, 1H), 8.75 (s, 1H), 7.72-7.65 (m, 6H), 7.42-

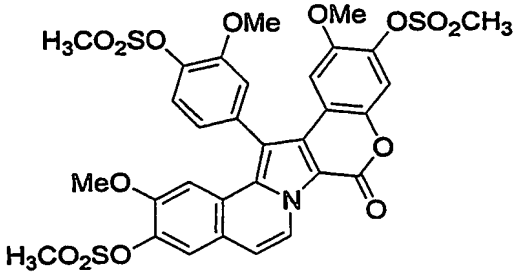
7.34 (m, 7H), 7.26-7.21 (m, 3H), 7.23 (s, 1H), 6.85 (s, 1H), 6.81 (s, 1H), 4.93-4.86 (m, 1H), 4.78-4.69 (m, 1H), 3.84 (s, 3H), 3.50 (s, 3H), 3.44 (s, 3H), 3.15 (br t, 2H). MS (ESI) m/z: 1040 $(M+23)^+$. Rf: 0.24 ($CH_2Cl_2$:MeOH, 50:1).

Example 63: Compound 63



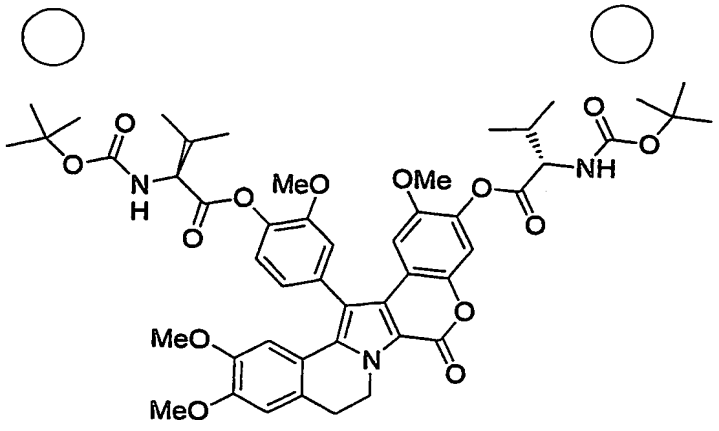

TFA (1 mL) was added to a solution of 21 (20.0 mg, 0.0233 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x2 mL) and evaporated to dryness to give 63 as a white solid (31.9 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.44-7.38 (m, 2H), 7.24-7.20 (m, 2H), 6.94 (br s, 1H), 6.82-6.78 (m, 1H), 6.71-6.68 (m, 1H), 4.72(m, 1H), 4.49-4.38 (m, 2H), 3.44 (s, 3H), 3.35 (s, 6H), 3.30 (s, 3H), 3.13 (br t, 2H), 1.77 (br d, 3H), 1.70 (br d, 3H). MS (ESI) m/z: 658 $(M+1)^+$.

Example 64: Compound 64



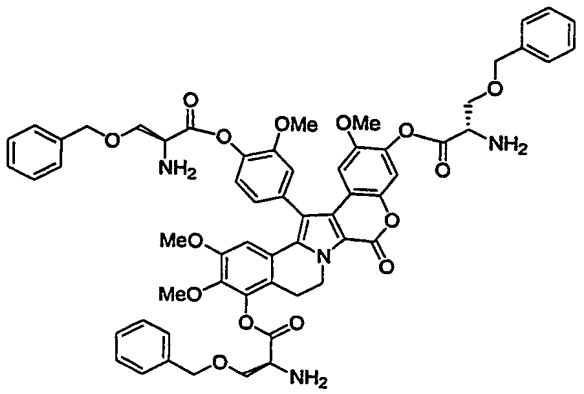

A suspension of 22 (25 mg, 0.034 mmol) and DDQ (15 mg, 0.068 mmol) in $CHCl_3$ (2 mL) was refluxed for 77 h. The mixture was cooled to 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 80:1) to give 64 (17 mg, 68%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.16 (d, $J$= 7.5 Hz, 1H), 7.66 (s, 1H), 7.60 (d, $J$= 8.6 Hz, 1H), 7.33-7.30 (m, 3H), 7.18 (s, 1H), 7.06 (d, $J$= 7.7 Hz, 1H), 6.76 (s, 1H), 3.96 (s, 3H), 3.49 (s, 6H), 3.37 (s, 3H), 3.24 (s, 3H), 3.21 (s, 3H). MS (ESI) m/z: 734 $(M+1)^+$. Rf: 0.33 ($CH_2Cl_2$:MeOH, 80:1).

Example 65: Compound 65



A suspension of **95** (50.0 mg, 0.097 mmol), (L)-N-Boc-valine (84.3 mg, 0.388 mmol), EDC·HCl (74.4 mg, 0.388 mmol) and DMAP (5.0 mg, 0.04 mmol) in anhydrous $CH_2Cl_2$ (10 mL) was stirred at 23 °C for 3 h under Argon atmosphere. The reaction mixture was diluted with EtOAc (50 mL) and washed with $H_2O$ (50 mL) and with saturated aqueous solution of $NaHCO_3$ (50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give **65** as a white solid (83.6 mg, 94%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.25-7.09 (m, 4H), 6.76 (br s, 1H), 6.71-6.66 (m, 2H), 5.06 (br d, $J$= 9.3 Hz, 1H), 4.91-4.71 (m, 2H), 4.53-4.50 (m, 2H), 3.89 (s, 3H), 3.77 (s, 3H), 3.40 (s, 6H), 3.13 (t, $J$= 7.3 Hz, 2H), 2.41-2.37 (m, 2H), 1.47 (d, $J$= 6.1 Hz,18 H), 1.12-0.99 (m, 12H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.3, 155.6 (2C), 154.9, 151.9, 149.1, 147.6, 147.4, 144.8, 139.5, 138.4, 135.7, 134.4, 127.1, 127.0, 126.4, 123.7, 123.3, 119.5, 116.2, 114.8, 114.6, 114.4, 111.7, 110.9, 108.5, 105.4, 79.9 (2C), 58.5 (2C), 55.9, 55.8, 55.5, 55.4, 42.4, 31.2, 31.1, 28.5, 28.2 (6C), 19.1, 18.9, 17.1, 17.0. MS (ESI) m/z: 936 $(M+23)^+$, 914 $(M+1)^+$. Rf: 0.22 ($CH_2Cl_2$:MeOH, 60:1).

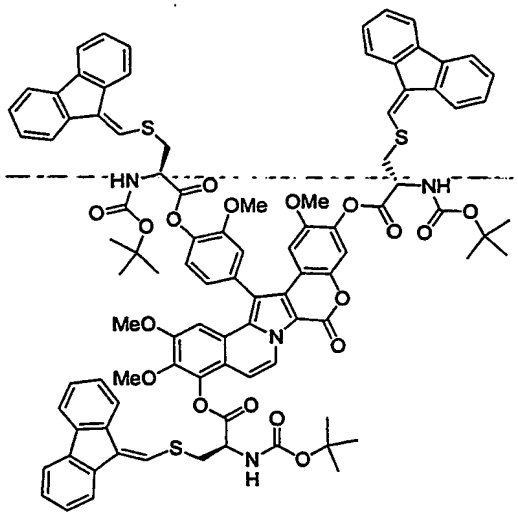
Example 66: Compound **66**



TFA (1 mL) was added to a solution of **68** (18 mg, 0.013 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **66** was obtained as a white solid (18 mg, quant.). The solid was collected by triturating in ethyl ether and filtrating. $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.50-7.20 (m, 17H), 7.16-7.12 (m, 2H), 6.80-6.75 (m, 2H), 4.80-4.60 (m, 11H), 4.35-3.95 (m, 6H),

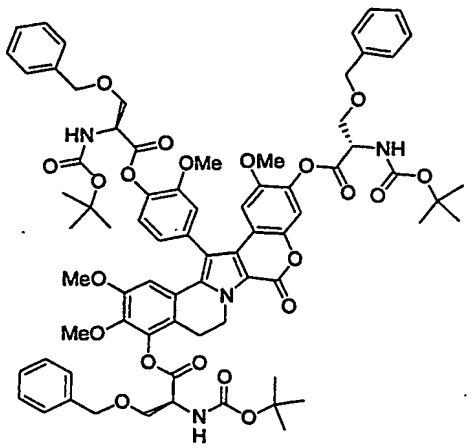
3.78 (s, 3H), 3.76 (s, 3H), 3.39 (d, $J$= 2.1 Hz, 3H), 3.36 (d, $J$= 2.1 Hz, 3H), 2.91 (br s, 2H). MS (ESI) m/z: 1063 $(M)^+$.

Example 67: Compound **67**



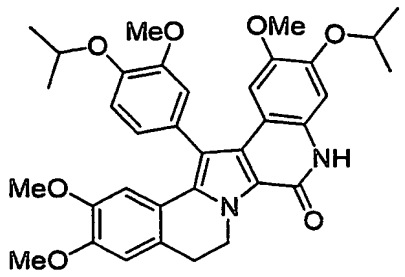
To a solution of **114** (64 mg, 0.038 mmol) in $CHCl_3$ (2 mL), DDQ (17 mg, 0.076 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 70 h. The reaction was followed by $^1H$ NMR. The reaction was cooled to 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel (hexane:EtOAc, 50:50) to give **67** as a brownish solid (52 mg, 81%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.06 (d, $J$= 7.5 Hz, 1H), 8.10-8.00 (m, 3H), 7.80-7.65 (m, 6H), 7.60-7.50 (m, 3H), 7.50-7.10 (m, 21H), 6.74 (s, 1H), 5.80-5.50 (m, 3H), 5.20-5.00 (m, 3H), 3.91 (s, 3H), 3.81 (s, 3H), 3.80-3.60 (m, 6H), 3.50-3.40 (m, 6H), 1.49 (s, 18H), 1.45 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.8, 168.4, 168.3, 168.2, 155.1, 154.9, 154.6, 153.1, 153.0, 152.0, 147.3, 145.3, 141.5, 140.2, 140.1, 140.0, 139.6, 139.0, 138.5, 138.1, 138.0, 136.7, 134.8, 132.9, 132.7, 132.5, 128.0, 127.9, 127.8, 127.7, 127.5, 127.3, 127.2, 127.1, 127.0, 126.9, 126.8, 126.7, 125.9, 125.3, 125.2, 123.8, 123.6, 123.5, 120.8, 119.9, 119.8, 119.7, 119.4, 119.2, 119.1, 117.9, 116.0, 115.1, 112.0, 111.9, 109.0, 106.6, 106.1, 104.4, 80.9, 80.8, 80.7, 61.0, 56.2, 55.8, 55.7, 55.6, 54.3, 54.1, 38.8, 29.7, 28.3, 28.2, 27.3. MS (ESI) m/z: 1689 $(M+23)^+$. Rf: 0.19 (hexane:EtOAc, 2:1).

Example 68: Compound **68**



A suspension of 1 (60 mg, 0.11 mmol), (L)-N-Boc-Ser(Bzl) (200 mg, 0.67 mmol), EDC·HCl (130 mg, 0.67 mmol) and DMAP (8 mg, 0.067 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was quenched with $H_2O$ (20 mL), diluted with EtOAc (50 mL), washed with $H_2O$ (2x20 mL) and saturated aqueous solution of $NaHCO_3$ (2x20 mL), dried over $Na_2SO_4$, filtered, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give 68 as a white solid (153 mg, quant.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.40-7.25 (m, 15H), 7.20-7.05 (m, 4H), 6.70-6.65 (m, 2H), 5.60-5.45 (m, 3H), 4.80-4.50 (m, 11H), 4.20-4.00 (m, 3H), 3.90-3.80 (m, 3H), 3.74 (s, 6H), 3.36 (t, $J$= 4.7 Hz, 6H), 2.89 (br s, 2H), 1.48 (s, 18H), 1.46 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.0, 168.8, 155.4, 155.3, 154.9, 152.1, 151.8, 147.5, 144.8, 141.3, 141.1, 139.7, 138.6, 137.4, 137.0, 134.7, 134.3, 128.6, 128.5, 128.4, 128.2, 127.8, 127.6, 127.5, 126.9, 123.8, 123.1, 122.8, 119.4, 116.1, 115.6, 114.7, 111.8, 107.6, 105.5, 80.2, 80.1, 80.0, 73.7, 73.4, 70.0, 69.9, 60.8, 60.3, 56.1, 55.7, 55.5, 54.2, 54.1, 54.0, 41.8, 28.2, 22.0. MS (ESI) m/z: 1385 $(M+23)^+$. Rf: 0.59 (hexane:EtOAc, 50:50).

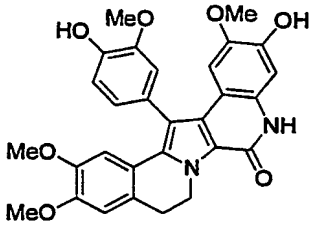
Example 69: Compound 69



6,7-Dimethoxy-3,4-dihydroisoquinoline (14.2 mg, 0.074 mmol) was added to a solution of LL-10-amide (40.0 mg, 0.074 mmol) in dry dimethylacetamide (2 mL) under Argon atmosphere. The solution was stirred at 23 °C for 24 h, then $Et_3N$ (10 mL, 0.074 mmol) was added and the reaction mixture was heated at 80 °C for 18 h. The solution was cooled to 23 °C, then $(KSO_3)_2NO$ (19.9 mg, 0.074 mmol) and saturated aqueous solution of $Na_2CO_3$ (1 mL) was added and the suspension was stirred for 1 h. After this time, the mixture was treated with saturated aqueous solution of $NaHCO_3$ and extracted with $CH_2Cl_2$. The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvent was evaporated under reduced pressure. The resulted residue was purified by

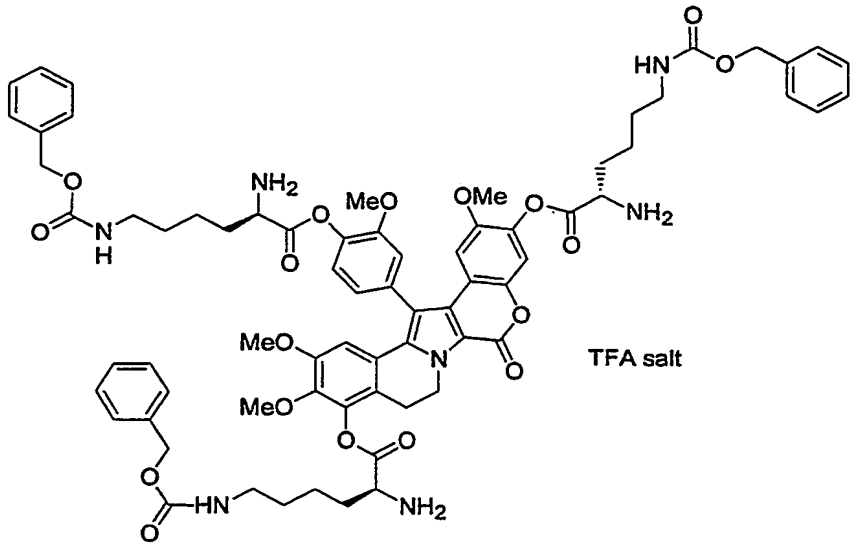
chromatography on silica gel (EtOAc) to afford **69** compound as a white solid (4.2 mg, 9%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.71 (br s, 1H), 7.10 (br s, 2H), 7.07 (s, 1H), 6.81 (s, 1H), 6.78 (s, 1H), 6.76 (m, 2H), 5.03-4.94 (m, 2H), 4.61-4.55 (m, 2H), 3.89 (s, 3H), 3.82 (s, 3H), 3.41 (s, 3H), 3.37 (s, 3H), 3.12 (t, $J$= 6.8 Hz, 2H), 1.40 (d, $J$= 5.9 Hz, 12H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 156.6, 151.2, 148.3, 147.3, 146.6, 145.8, 133.6, 129.7, 127.3, 126.3, 123.5, 120.7, 118.6, 116.9, 114.8, 114.5, 111.1, 110.9, 108.5, 105.1, 102.5, 71.7, 71.4, 56.0, 55.8, 55.1, 55.0, 42.3, 29.0, 21.9 (2C), 20.9 (2C). MS (ESI) m/z: 599 $(M+1)^+$. Rf: 0.21 (EtOAc).

Example 70: Compound **70**




A suspension of **69** (3.1 mg, 0.005 mmol) and $AlCl_3$ (2.7 mg, 0.02 mmol) in anhydrous $CH_2Cl_2$ (2 mL) was stirred from 0 °C to 23 °C for 3 h under Argon atmosphere. MeOH (1 mL) was added and the solvent was evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel (EtOAc) to afford **70** compound as a white solid (2.4 mg, 94 %). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.26 (br s, 1H), 7.12-7.07 (m, 2H), 7.00 (s, 1H), 6.79-6.73 (m, 4H), 5.75 (s, 2H), 5.15-5.11 (m, 1H), 4.81 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.49 (s, 3H), 3.39 (s, 3H), 3.13-3.11 (m, 2H). MS (ESI) m/z: 515 $(M+1)^+$. Rf: 0.41 ($CH_2Cl_2$:MeOH, 10:1).

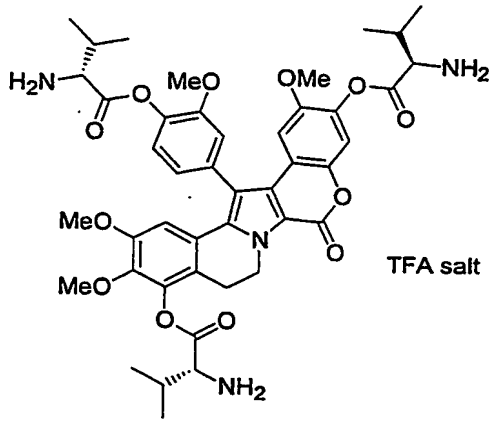
Example 71: Compound **71**




TFA (1 mL) was added to a solution of **74** (10.4 mg, 0.0064 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x5 mL) and evaporated to dryness to give

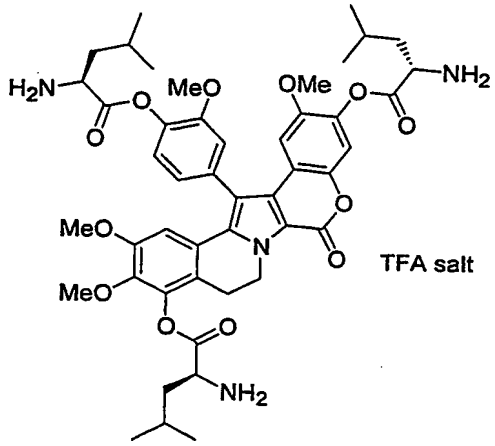
**71** as a white solid (14.0 mg, quant.) $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.45-7.22 (m, 19H), 6.80-6.74 (m, 2H), 5.08 (m, 1H), 5.03 (s, 6H), 4.78 (m, 1H), 4.51 (br t, 1H), 4.42 (br t, 1H), 4.35 (br t, 1H), 3.79 (s, 6H), 3.42 (s, 3H), 3.41 (s, 3H), 3.21 (br s, 6H), 3.05 (m, 2H), 2.15 (m, 6H), 1.65 (m, 12H). MS (ESI) m/z: 1340 $(M+23)^+$, 1318 $(M+1)^+$.

Example 72: Compound **72**




TFA (1 mL) was added to a solution of **75** (11.6 mg, 0.0102 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x5 mL) and evaporated to dryness to give **72** as a white solid (14.1 mg, quant.) $^1$H NMR (300 MHz $CD_3OD$) $\delta$ 7.48-7.42 (m, 2H), 7.28-7.20 (m, 2H), 6.83-6.77 (m, 2H), 4.76 (m, 2H), 4.45 (dd, J= 4.4, 2.0 Hz, 1H), 4.33 (dd, *J*= 4.4, 2.0 Hz, 1H), 4.23 (dd, *J*= 4.4, 2.0 Hz, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.44 (s, 3H), 3.43 (s, 3H), 3.05 (m, 2H), 2.59-2.44 (m, 3H), 1.38-1.20 (m, 18H). MS (ESI) m/z: 829 $(M+1)^+$. Rf: 0.28 ($CH_2Cl_2$:MeOH, 10:1).

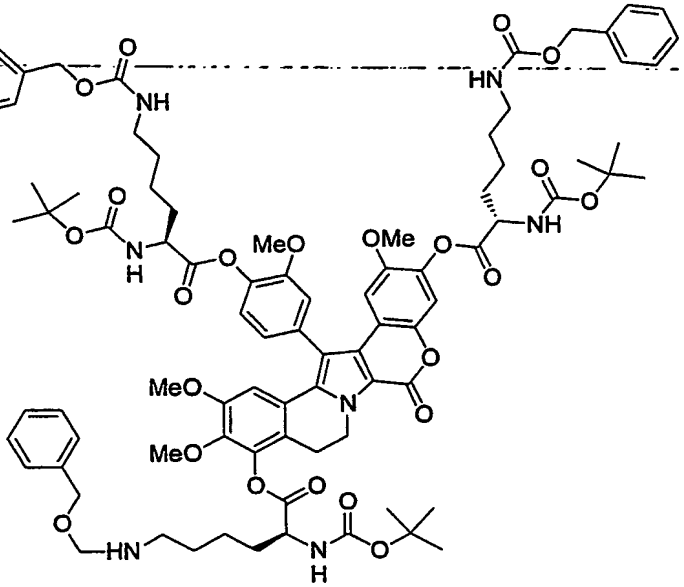
Example 73: Compound **73**




TFA (1 mL) was added to a solution of **76** (10.4 mg, 0.0089 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x5 mL) and evaporated to dryness to give

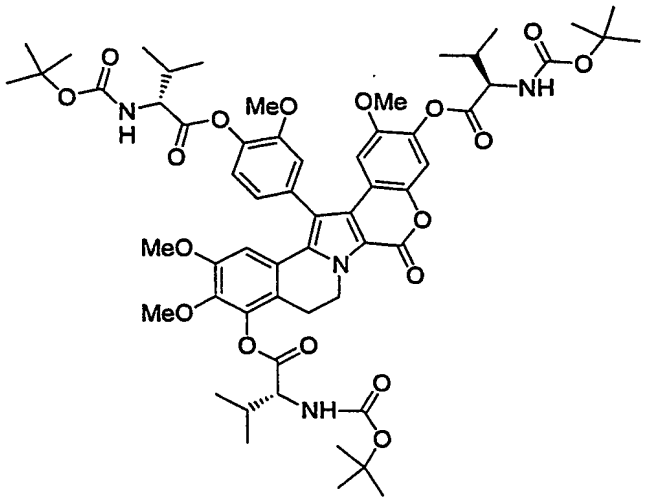
**73** as a white solid (13.8 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.47-7.41 (m, 2H), 7.31-7.21 (m, 2H), 6.81-6.77 (m, 2H), 4.90-4.76 (m, 2H), 4.48 (t, $J$= 7.3 Hz, 1H), 4.40 (t, $J$= 7.1 Hz, 1H), 4.42 (t, $J$= 6.6 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.44 (s, 3H), 3.42 (s, 3H), 3.17-3.06 (m, 2H), 2.14-1.77 (m, 9H), 1.12-1.00 (m, 18H). MS (ESI) m/z: 871 $(M+1)^+$. Rf: 0.3 ($CH_2Cl_2$:MeOH, 10:1).

Example 74: Compound **74**



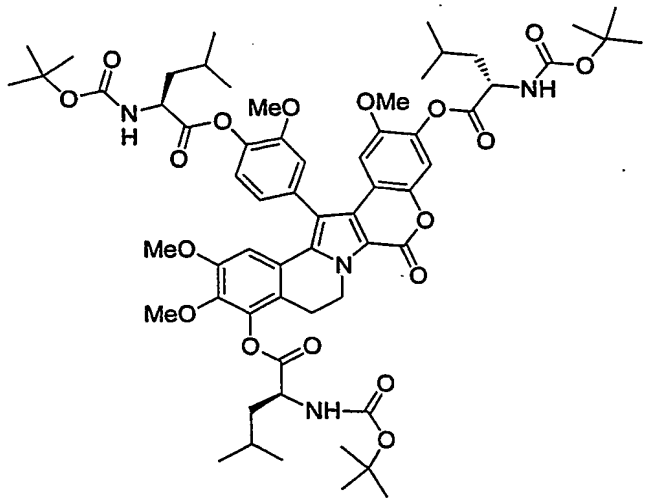

A suspension of **1** (50.0 mg, 0.094 mmol), (L)-N-Boc-Lysine-CBz (214.7 mg, 0.564 mmol), EDC·HCl (108.2 mg, 0.564 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 5 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) and then a second one (hexane:EtOAc, 2:3) to give **74** as a yellow solid (114.6 mg, 75 %). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.34 -7.31 (m, 15H), 7.15-7.07 (m, 4H), 6.67-6.63 (m, 2H), 5.08 (br s, 6H), 4.92 (m, 3H), 4.55 (m, 2H), 3.77 (s, 6H), 3.39 (s, 3H), 3.37 (s, 3H), 3.26-3.17 (m, 6H), 3.00 (br t, 2H), 2.04-1.76 (m, 6H), 1.58-1.29 (m, 38H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 170.7 (2C), 156.5, 156.4, 155.5, 155.3 (2C), 154.8, 152.0, 151.7, 147.4 (2C), 144.8, 144.7, 141.2 (2C), 140.9 (2C), 139.6, 138.4 (2C), 136.5, 136.4, 134.7, 134.6, 134.2, 128.4, 128.0, 126.9, 126.8, 123.7, 123.2, 122.6, 119.4 (2C), 116., 115.6, 114.7(2C), 111.7, 1107.6, 105.4 (2C). MS (ESI) m/z: 1640 $(M+23)^+$. Rf: 0.30 (hexane:EtOAc, 2:3).

Example 75: Compound **75**



A suspension of **1** (50.0 mg, 0.094 mmol), (D)-N-Boc-Valine (122.6 mg, 0.564 mmol), EDC·HCl (108.2 mg, 0.564 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 5 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give **75** as a yellow solid (96.5 mg, 91%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.23 (s, 1H), 7.17-7.15 (m, 1H), 7.10-7.09 (m, 2H), 6.69-6.40 (m, 2H), 5.05 (br t, $J$= 8.1 Hz, 2H), 4.53-4.51 (m, 3H), 3.78 (s, 6H), 3.40 (s, 3H), 3.38 (s, 3H), 3.01 (br t, 2H), 2.40-2.38 (m, 3H), 1.49 (br s, 27H), 1.15-0.99 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.5, 170.3, 155.7, 155.6 (2C), 154.9, 152.0, 151.8, 147.5, 144.8, 141.2, 141.0, 139.6, 138.5, 134.8, 134.3, 127.0, 126.9, 123.8, 123.2, 122.6, 119.4, 116.1, 115.6, 114.8, 114.7, 111.8, 107.6, 105.4, 80.1, 79.9 (2C), 58.9, 58.5 (2C), 56.0 (2C), 55.5 (2C), 41.8, 31.2, 31.1, 30.8, 28.2 (9C), 22.2, 19.2, 19.1, 18.9, 17.4, 17.1, 17.0. MS (ESI) m/z: 1129 $(M+1)^+$. Rf: 0.23 (hexane:EtOAc, 2:1).

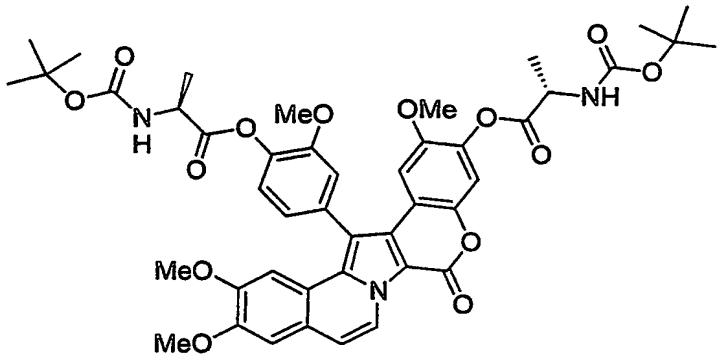
Example 76: Compound **76**



A suspension of **1** (50.0 mg, 0.094 mmol), (L)-N-Boc-Leucine (130.5 mg, 0.564 mmol), EDC·HCl (108.2 mg, 0.564 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5

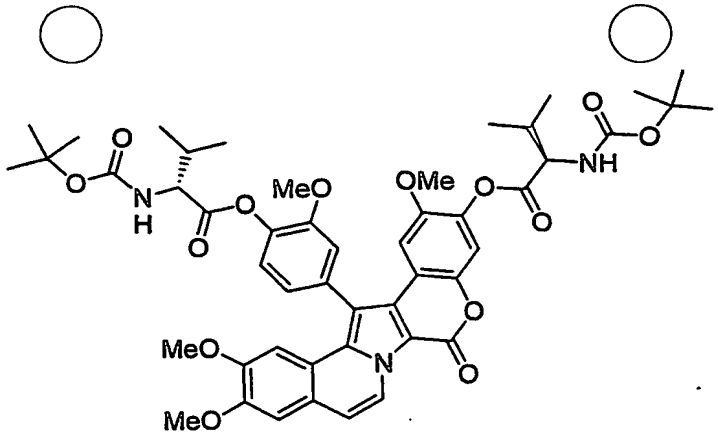
mL) was stirred at 23 °C for 5 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give 76 as a yellow solid (100.1 mg, 91%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.24-7.08 (m, 4H), 6.68-6.64 (m, 2H), 4.92 (m, 2H), 4.57 (m, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.40 (s, 3H), 3.39 (s, 3H), 3.02 (br t, 2H), 1.87-1.85 (m, 2H), 1.87-1.85 (m, 3H), 1.70-1.61 (m, 3H), 1.58 (br s, 27 H), 1.05-0.98 (m, 18 H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.4 (2C), 155.5, 155.4, 155.3, 155.0, 152.1, 151.8, 147.5, 144.8, 141.4, 141.0, 139.8, 138.7, 134.8, 134.2, 127.1, 123.8, 123.2, 122.7, 119.5, 116.1, 115.7, 114.7 (2C), 111.8, 107.6, 105.4 (2C), 80.2, 80.0 (2C), 60.7, 56.1, 55.7, 55.5, 52.3 (3C), 41.9, 41.6, 41.5, 41.2, 29.6, 28.3 (9C), 24.7 (3C), 22.9 (2C), 22.8 (2C), 22.7, 21.8. MS (ESI) m/z: 1193 $(M+23)^+$, 1171 $(M+1)^+$. Rf: 0.29 (hexane:EtOAc, 2:1).

Example 77: Compound 77



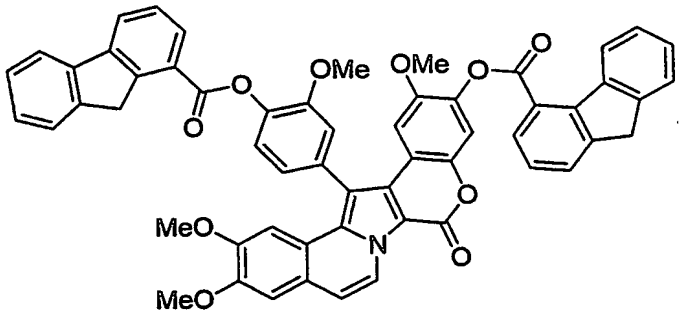

A suspension of 26 (12.0 mg, 0.0233 mmol), (L)-N-Boc-Alanine (17.6 mg, 0.0932 mmol), EDC·HCl (17.9 mg, 0.0932 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give 77 as a white solid (12.4 mg, 62%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.24 (d, $J$= 7.6 Hz, 1H), 7.34-7.08 (m, 7 H), 6.74 (d, $J$= 8.1 Hz, 1H), 5.30-5.12 (m, 2H), 4.62-4.60 (m, 2H), 4.00 (s, 3H), 3.80 (s, 3H), 3.51 (s, 3H), 3.44 (s, 3H), 1.64-1.44 (m, 24H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.5, 155.0, 152.2, 150.3, 149.6, 147.5, 145.5, 140.0, 139.4, 134.8, 134.2 (2C), 128.3 (2C), 124.7, 123.8, 123.2. 119.0, 116.0, 115.3, 113.0, 112.0, 110.9, 108.4, 107.5, 106.2, 105.1, 80.1, 56.2, 56.0, 55.8, 55.7, 49.3, 28.3, 18.7. MS (ESI) m/z: 878 $(M+23)^+$, 856 $(M+1)^+$. Rf: 0.13 ($CH_2Cl_2$:MeOH, 60:1).

Example 78: Compound 78



A suspension of 26 (12.0 mg, 0.0233 mmol), (D)-N-Boc-Valine (20.2 mg, 0.0932 mmol), EDC·HCl (17.9 mg, 0.0932 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give 78 as a white solid (15.4 mg, 86%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$= 7.3 Hz, 1H), 7.32-7.22 (m, 3H), 7.14-7.07 (m, 4H), 6.6.80 (d, $J$= 8.8 Hz, 1H), 5.09-5.06 (m, 2H), 4.57-4.52 (m, 2H), 3.99 (s, 3H), 3.80 (s, 3H), 3.51 (s, 3H), 3.43 (s, 3H), 2.46-2.38 (m, 2H),1.49-1.45 (m, 18H), 1.27-1.00 (m, 12H). MS (ESI) m/z: 934 $(M+23)^+$, 912 $(M+1)^+$. Rf: 0.32 ($CH_2Cl_2$:MeOH, 60:1).

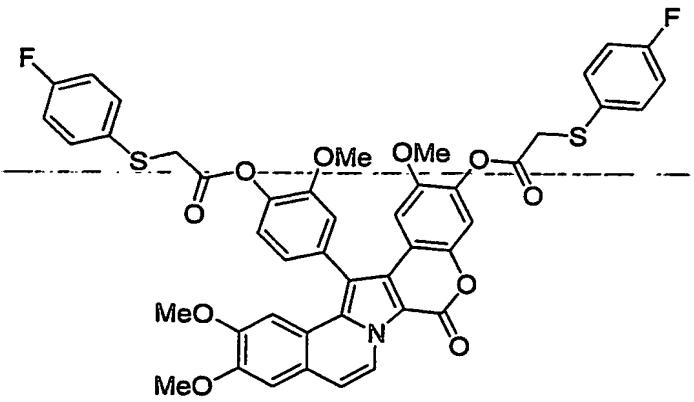
Example 79: Compound 79



A suspension of 26 (12.0 mg, 0.0233 mmol), 9H-fluorene-4-carboxilic acid (19.6 mg, 0.0932 mmol), EDC·HCl (17.9 mg, 0.0932 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, from 2:1 to 1:1). A second short chromatography was neccesary to purified the residue on silica gel ($CH_2Cl_2$) to give 79 as a white solid (8.6 mg, 41%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.31 (d, $J$= 7.3 Hz, 1H), 8.53-8.45 (m, 2H), 8.20 (d, $J$= 7.8 Hz, 1H), 8.2 (d, $J$= 8.0 Hz, 1H),7.71 (t, $J$= 7.1 Hz, 2H), 7.61-7.53 (m, 3H), 7.47-7.32 (m, 10H), 7.16-7.13 (m, 2H), 7.05 (s, 1H), 4.02 (s, 3H), 3.99 (s, 2H), 3.96 (s, 2H), 3.90 (s, 3H), 3.66 (s, 3H), 3.61 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 166.0, 165.9, 155.2, 152.6, 150.4, 149.6, 148.0, 145.7, 145.2, 145.1, 144.3, 144.2, 141.6, 141.4, 140.5, 140.0, 139.9 (2C), 134.8, 134.3, 129.6, 129.4, 129.1 (2C), 128.5, 127.8, 127.7, 126.9, 126.7, 126.1, 126.0, 125.4, 125.1, 125.0, 124.9, 124.8 (2C), 124.6, 124.2, 124.0, 123.2,

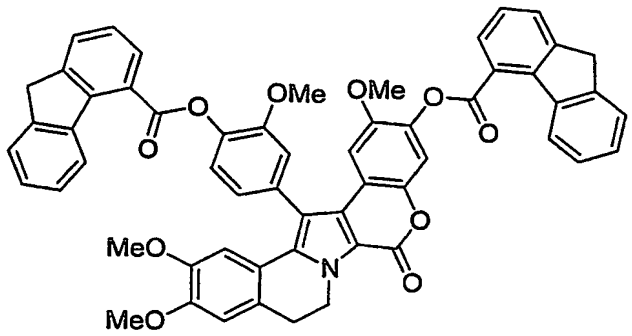
119.1, 116.1, 115.4, 113.0, 112.4, 111.2, 108.5, 107.5, 106.4, 105.2, 56.3, 56.0, 55.9, 55.9, 37.0 (2C). MS (ESI) m/z: 898 $(M+1)^+$. Rf: 0.50 (hexane:EtOAc, 50:50).

Example 80: Compound **80**




A suspension of **26** (12.0 mg, 0.0233 mmol), 2[(4-fluorophenyl)thio]acetic acid (17.9 mg, 0.0932 mmol), EDC·HCl (17.4 mg, 0.0932 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give **80** as a white solid (20.4 mg, quant.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$= 7.3 Hz, 1H), 7.58-7.50 (m, 4H), 7.26-7.20 (m, 4H), 7.11-7.01 (m, 8H), 6.78 (s, 1H), 4.00 (s, 3H), 3.87 (s, 2H), 3.81 (s, 2H), 3.77 (s, 3H), 3.48 (s, 3H), 3.37 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 167.5, 164.2, 161.0, 154.9, 152.1, 150.3, 149.5, 147.5, 145.4, 139.9, 139.3, 134.9, 134.2, 133.9, 133.8, 133.8, 133.7, 129.3, 128.1, 125.0, 124.7, 123.8, 123.6, 123.1, 118.9, 116.4, 116.1, 115.4, 113.0, 111.9, 110.8, 108.4, 107.5, 106.2, 105.0, 56.2, 56.0, 55.6, 55.5, 37.5, 37.4. MS (ESI) m/z: 872 $(M+23)^+$, 850 $(M+1)^+$. Rf: 0.52 (hexane:EtOAc, 2:1).

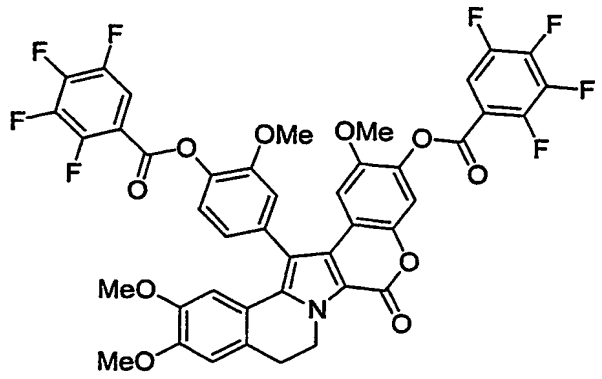
Example 81: Compound **81**




A suspension of **95** (12.2 mg, 0.0236 mmol), 9H-fluorene-4-carboxilic acid (19.8 mg, 0.094 mmol), DCC (19.5 mg, 0.094 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 200:1) to give **81** as a yellow solid (20.0 mg, 95%). $^1H$ NMR (300

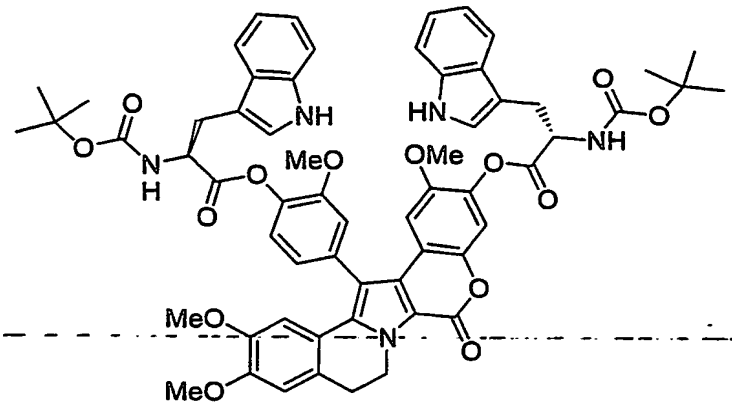
MHz, $CDCl_3$) $\delta$ 8.53-8.43 (m, 2H), 8.17 (m, 2H), 7.78-7.41 (m, 2H), 1.10-1.30 (m, 12H), 6.94 (s, 1H), 6.83 (s, 1H), 6.80 (s, 1H), 4.96-4.80 (m, 2H), 3.98 (s, 2H), 3.96 (s, 2H), 3.93 (s, 3H), 3.88 (s, 3H), 3.60 (s, 3H), 3.54 (s, 3H), 3.19 (t, $J$= 6.1 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 165.9, 155.2, 152.5, 149.2, 147.9, 147.8, 145.2, 145.1, 144.3, 144.1, 141.5, 141.3, 140.3, 139.9, 139.1, 136.0, 134.5, 129.5, 129.3, 129.0, 127.7, 127.6, 127.4, 127.3, 127.2, 126.8, 126.7, 126.6, 126.5, 126.1, 126.0, 125.9, 125.4, 125.2, 125.1, 125.0,124.7, 124.5, 124.0, 123.5, 121.5, 119.7, 116.3, 115.0, 114.5, 112.1, 111.0, 108.6, 105.7, 56.2, 55.9, 55.9, 55.6, 42.6, 37.0 (2 C), 28.6. MS (ESI) m/z: 922 $(M+23)^+$, 900 $(M+1)^+$. Rf: 0.44 ($CH_2Cl_2$:MeOH, 200:1).

Example 82: Compound **82**



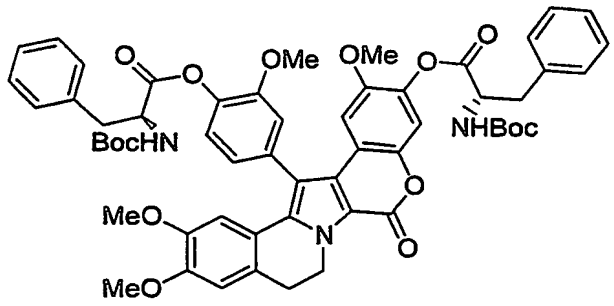

A suspension of **803** (12.2 mg, 0.0236 mmol), 2,3,4,5-tetrafluorobenzoic acid (18.3 mg, 0.094 mmol), DCC (19.5 mg, 0.094 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 200:1) to give **82** as a yellow solid (20.7 mg, quant). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.81-7.76 (m, 2H), 7.35 (d, $J_{H-F}$= 7.8 Hz, 1H), 7.25-7.20 (m, 3H), 6.79 (br s, 2H), 6.71 (s, 1H), 4.92-4.79 (m, 2H), 3.91 (s, 3H), 3.82 (s, 3H), 3.48 (s, 3H), 3.46 (s, 3H), 3.16 (t, $J$= 7.3 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 159.7 (2C), 155.0, 152.0, 150.2 (m), 149.3, 148.2 (m), 147.7, 147.4, 146.7 (m), 145.8 (m), 145.0 (m), 144.9, 143.4 (m), 142.3 (m), 140.0 (m), 139.4, 138.2, 136.0, 135.0, 127.0, 126.6, 123.6, 123.5, 119.5, 116.7, 115.1, 114.7, 114.6, 13.6 (m), 113.6(m), 111.8, 111.0, 108.5, 105.6, 56.3, 55.9, 55.8, 55.5, 42.5, 28.6. MS (ESI) m/z: 889 $(M+23)^+$, 867 $(M+1)^+$. Rf: 0.25 ($CH_2Cl_2$:MeOH, 200:1)

Example 83: Compound **83**



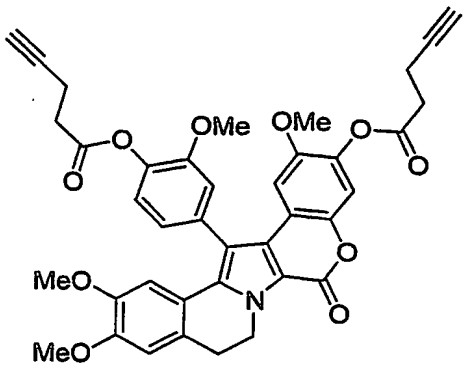
A suspension of **95** (6.3 mg, 0.0122 mmol), (L)-N-Boc-Tryptophane (12.5 mg, 0.0488 mmol), DCC (10.1 mg, 0.0488 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 6 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 25:1) to give **83** as a yellow solid (13.0 mg, 98%).$^1$H NMR (300 MHz, $CDCl_3$) $\delta$8.25-8.23 (br d, 2H), 7.68-7.63 (m, 2H), 7.40-7.34 (m, 2H), 7.26-7.05 (m, 7H), 6.93 (s, 1H), 6.77 (s, 1H), 6.67 (br s, 2H), 4.95-4.74 (m, 4H), 3.90 (s, 3H), 3.75 (s, 3H), 3.57-3.50 (m, 4H), 3.82 (s, 3H), 3.36 (s, 3H), 3.13 (br t, $J$= 6.6 Hz, 2H), 1.43 (br d, 18H). MS (ESI) m/z: 1110 $(M+23)^+$. Rf: 0.11 ($CH_2Cl_2$:MeOH, 30:1).

Example 84: Compound **84**



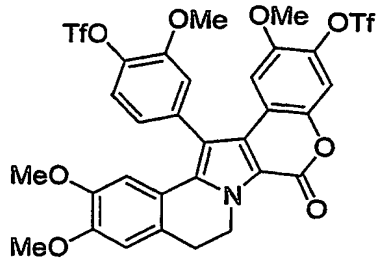
A suspension of **95** (7.0 mg, 0.0135 mmol), (L)-N-Boc-Phenylalanine (14.3 mg, 0.054 mmol), DCC (11.1 mg, 0.054 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give **84** as a yellow solid (13.0 mg, 96%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$7.36-7.20 (m, 9H), 7.17-7.04 (m, 5H), 6.77 (s, 1H), 6.79-6.66 (m, 2H), 5.02-4.74 (m, 4H), 3.90 (s, 3H), 3.80 (s, 3H), 3.40 (s, 3H), 3.39 (s, 3H), 3.34 - 3.12 (m, 6H), 1.44-138 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$169.9, 154.9, 151.9, 149.1, 147.6, 147.4, 144.7, 139.4, 138.3, 135.8, 134.4, 129.4, 129.2, 128.5, 127.1, 126.4, 126.3, 123.6, 123.3, 119.5, 116.3, 114.9, 114.6, 114.4, 111.7, 110.9, 108.4, 105.4, 79.9,79.9 (2C), 56.0, 55.8, 55.6, 55.4, 54.3 (2C), 42.4 38.0 (2C), 28.4, 28.2 (6C). MS (ESI) m/z: 1032 $(M+23)^+$. Rf: 0.76 ($CH_2Cl_2$:MeOH, 60:1).

Example 85: Compound **85**



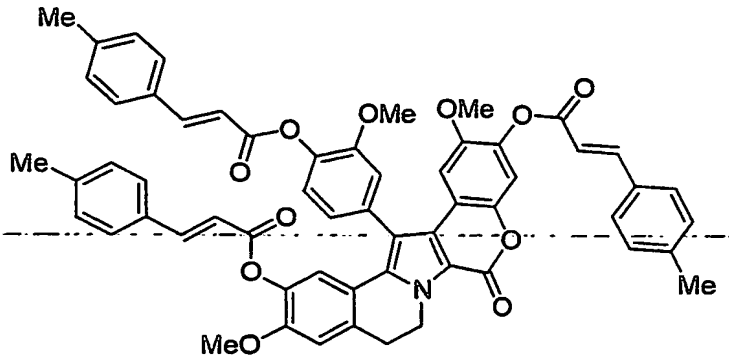

A suspension of **95** (7.0 mg, 0.0135 mmol), 4-pentynoic acid (8.7 mg, 0.054 mmol) , DCC (11.1 mg, 0.054 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 60:1) to give **85** as a yellow solid (9.0 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.26-7.21 (m, 2H), 7.15-7.10 (m, 2H), 6.76 (s, 1H), 6.71 (s, 1H), 6.68 (s, 1H), 4.89-4.3 (m, 2H), 3.89 (s, 3H), 3.42 (s, 3H), 3.42 (s, 3H), 3.40 (s, 3H), 3.23 (t, $J$= 7.1 Hz, 2H), 2.89-2.80 (m, 4H), 2.69-2.59 (m, 4H), 2.05-2.03 (m, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.7, 169.5, 155.1, 152.1, 149.1, 147.7, 147.6, 144.9, 139.8, 138.7, 135.9, 134.4, 130.9, 128.8, 127.2, 126.4, 123.8, 123.3, 119.6, 116.2, 114.8, 114.5, 111.9, 111.0, 108.5, 105.5, 82.1, 82.0, 69.3 (2C), 56.2, 55.9, 55.7, 55.4, 42.5, 33.1 (2C), 28.6. MS (ESI) m/z: 698 $(M+23)^+$, 676 $(M+1)^+$. Rf: 0.65 ($CH_2Cl_2$:MeOH, 60:1).

Example 86: Compound **86**



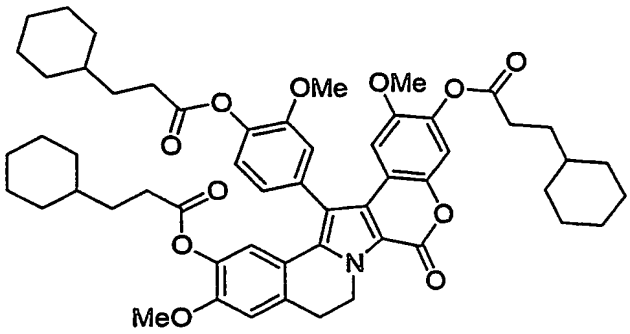

$Et_3N$ (15 μL, 0.1042 mmol) was added to a solution of **95** (7.0 mg, 0.0135 mmol) in $CH_2Cl_2$ (3 mL) a 0 °C under Argon atmosphere. $Tf_2NPh$ (20.7 mg, 0.058 mmol) and DMAP (0.5 mg, 0.0043 mmol) were addded and the mixture was stirred at 23 °C for 1 h. Saturated aqueous solution of $NaHCO_3$ (5 mL) was added and the mixture was extracted with $CH_2Cl_2$, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$) to give **86** as a yellow solid (13.4 mg, 89%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.45 (d, $J$= 8.8 Hz, 1H), 7.27 (s, 1H), 7.24-7.20 (m, 2H), 6.79 (s, 1), 6.66 (s, 1H), 6.54 (s, 1H), 4.93-4.86 (m, 1H), 4.77-4.70 (m, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.47 (s, 3H), 3.36 (s, 3H), 3.15 (br t, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.4, 152.5, 149.6, 147.8 (2C), 144.4, 138.5, 137.0 (3C), 136.2, 129.7, 126.8, 126.1, 123.6, 123.5, 118.6 (q, $J_{C-F}$= 136.7 Hz), 118.6 (q, $J_{C-F}$= 132.2 Hz), 115.7, 114.9, 114.0, 111.9, 111.2, 108.3, 105.7, 56.6, 56.0, 55.8, 55.2, 42.6, 28.5. MS (ESI) m/z: 780 $(M+1)^+$. Rf: 0.43 ($CH_2Cl_2$).

Example 87: Compound **87**



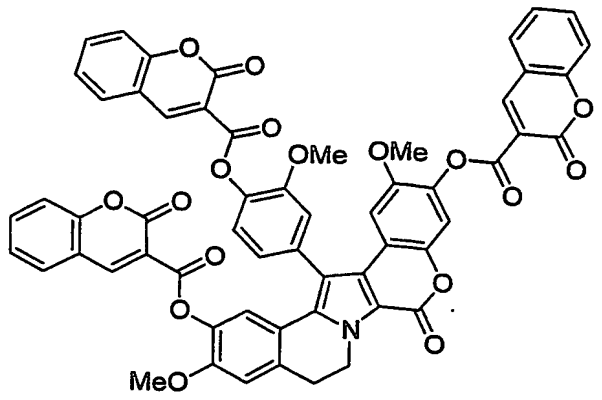

A suspension of **167** (3.5 mg, 0.0069 mmol), 4-methyl cinnamic acid (6.7 mg, 0.0414 mmol), DCC (8.5 mg, 0.0414 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 3 h under Argon atmosphere The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give **87** as a white solid (5.5 mg, 86%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.85 (d, $J$=16.4 Hz, 1H), 7.79 (d, $J$= 16.8 Hz, 1H), 7.75 (d, $J$= 15.8 Hz, 1H), 7.52-7.47 (m, 4H), 7.43-7.40 (m, 2H), 7.28-7.10 (m, 10H), 6.91 (s, 1H), 6.87 (s, 1H), 6.77 (s, 1H), 6.60 (d, $J$= 16.1 Hz, 1H), 6.58 (d, $J$= 16.1 Hz, 1H), 6.57 (d, $J$= 16.1 Hz, 1H), 4.96-4.90 (m, 1H), 4.82-4.78 (m, 1H), 3.87 (s, 3H), 3.81 (s, 3H), 3.50 (s, 3H), 3.21 (t, $J$= 7.1 Hz, 2H), 2.39 (s, 9H). MS (ESI) m/z: 956 $(M+23)^+$, 934 $(M+1)^+$. Rf: 0.45 (hexane:EtOAc, 50:50).

Example 88: Compound **88**



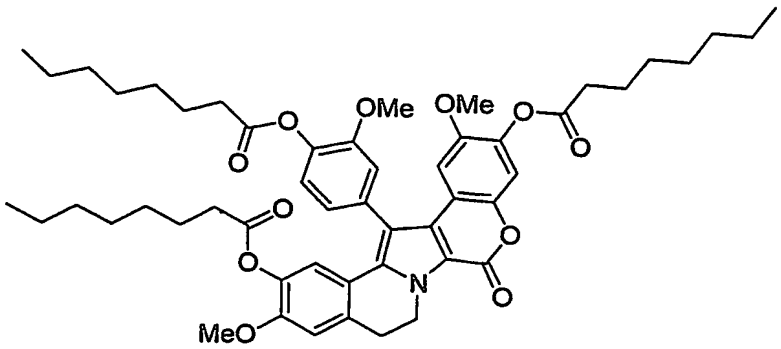

A suspension of **167** (2.5 mg, 0.0049 mmol), cyclohexyl propionic acid (5.0 mg, 0.0294 mmol), DCC (6.1 mg, 0.0294 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give **88** as a yellow oil (4.5 mg, quant.). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.19-7.15 (m, 1H), 7.08-7.03 (m, 3H), 6.86 (s, 1H), 6.72-6.69 (m, 2H), 4.93-4.87 (m, 1H), 4.76-4.71 (m, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.43 (s, 3H), 3.17 (br t, 2H), 2.64-2.55 (m, 6H), 1.77-1.40 (m, 21H), 1.36-1.02 (m, 12H), 0.98-0.88 (m, 6H). MS (ESI) m/z: 938 $(M+23)^+$, 916 $(M+1)^+$. Rf: 0.63 (hexane:EtOAc, 50:50).

Example 89: Compound 89




A suspension of 167 (5.0 mg, 0.0099 mmol), coumarin-3-carboxylic acid (11.3 mg, 0.0594 mmol), DCC (12.3 mg, 0.0594 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) and the yellow solid was triturated with MeOH to give 89 as a bright yellow solid (9.2 mg, 86%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.78 (s, 1H), 8.75 (s, 1H), 8.70 (s, 1H), 7.77-7.62 (m, 6H), 7.37-7.33 (m, 6H), 7.24-7.13 (m, 4H), 6.93 (s, 1H), 6.87 (s, 1H), 6.80 (s, 1H), 4.92 (m, 1H), 4.84 (m, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.50 (s, 3H), 3.23 (br t, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 160-8, 160.4 (2C), 156.5 (2C), 155.5, 155.4, 155.1, 152.1, 151.2, 150.3 (2C), 147.7, 144.9, 139.7, 138.6, 138.2, 134.9 (4C), 134.7, 133.9, 133.3, 130.2, 129.8 (2C), 127.1, 125.0, 124.9, 124.1, 123.2, 120.3, 120.1, 117.9, 117.8, 117.1, 116.9 (2C), 116.7, 116.5, 115.5, 114.8, 112.3, 112.1, 105.6, 56.3, 56.2 (2C), 42.2, 29.3. MS (ESI) m/z: 1017 $(M)^+$. Rf: 0.24 ($CH_2Cl_2$:MeOH, 40:1).

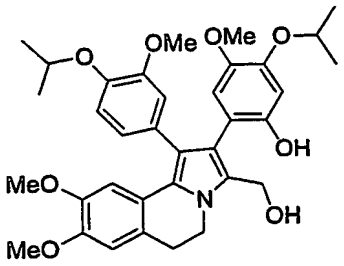
Example 90: Compound 90




A suspension of 167 (5.0 mg, 0.0099 mmol), octanoic acid (8.6 mg, 0.059 mmol), DCC (12.3 mg, 0.059 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give 90 as a yellow oil (7.8 mg, 90%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.18-7.15 (m, 1H), 7.08-7.02

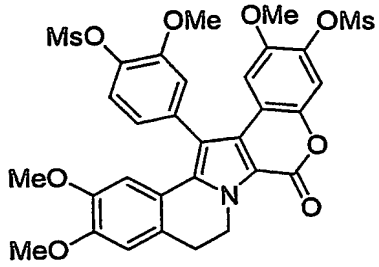
(m, 3H), 6.86 (s, 1H), 6.72-6.69 (m, 2H), 4.93-4.89 (m, 1H), 4.76-4.72 (m, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.43 (s, 3H), 3.17 (br t, 2H), 2.63-2.47 (m, 6H), 1.78-1.69 (m, 6H), 1.32-1.25 (m, 18H), 0.90-0.88 (m, 15H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.9, 171.7, 171.4, 155.2, 152.2, 151.2, 147.8, 144.9, 142.6, 140.0, 139.0, 138.5, 133.3, 132.7, 127.3, 123.9, 123.1, 123.0, 120.3, 116.0, 115.4, 114.6, 113.3, 112.1, 111.9, 105.5, 56.1, 55.9, 55.8, 42.2, 34.0, 33.9, 33.8, 31.7 (2C), 31.6, 29.2, 29.0, 28.9 (5C), 25.1, 24.9 (2C), 22.6 (3C), 14.1 (3C). MS (ESI) m/z: 902 $(M+23)^+$, 880 $(M+1)^+$. Rf: 0.38 (hexane: EtOAc, 2:1).

Example 91: Compound 91




A solution of 69 ( 6.0 mg, 0.01 mmol) was added to a suspension of $NaBH_4$ (1.0 mg, 0.02 mmol) in THF (2 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 3 h, then $H_2O$ ( 5 mL) was slowly added at 0 °C. The mixtured was extracted with $CH_2Cl_2$ (3x10 mL), dried over anhydrous $Na_2SO_4$, filtered, and evaporated under reduced pressure to give 91 as a white solid (6.0 mg, quant). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.84 (s, 1H), 6.80 (br s, 2H), 6.80 (s, 1H), 6.72 (s, 1H), 6.67 (s, 1H), 6.51 (s, 1H), 6.42 (s, 1H), 4.59 (s, 2H), 4.49-4.44 (m, 2H), 4-28-4.00 (m, 2H), 3.88 (s, 3H), 3.58 (s, 3H), 3.54 (s, 3H), 3.40 (s, 3H), 3.07 (m, 2H), 1.36 (d, $J$= 6.1 Hz, 6H), 1.31 (d, $J$= 6.1 Hz, 6H). MS (ESI) m/z: 626 $(M+23)^+$. Rf: 0.10 ($CH_2Cl_2$:MeOH, 20:1).

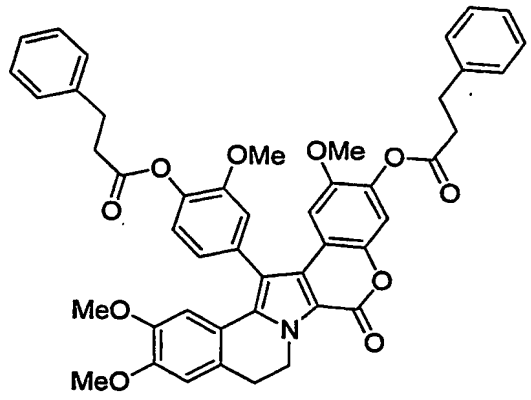
Example 92: Compound 92




A suspension of 95 (7.0 mg, 0.0135 mmol), methanesulfonyl chloride (6 mL, 0.077 mmol), pyridine (6 mL, 0.077 mmol) and DMAP (1 mg, 0.008 mmol) in $CH_2Cl_2$ (2 mL) was stirred at 23 °C for 48 h under Argon atmosphere. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to give 92 as a yellow solid (7.5 mg, 83%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.50 (d, $J$= 8.1 Hz, 1H), 7.32 (br s, 1H), 7.21 (br d, $J$= 8.1 Hz, 1H), 7.14 (br s, 1H), 6.77 (s, 1H), 6.68 (s, 1H), 6.61 (s, 1H), 4.99-4.94 (m, 1H), 7.70-4.66 (m, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.46 (s, 3H), 3.37 (s, 3H), 3.31 (s, 3H), 3.19 (s, 3H), 3.12 (br t, $J$= 6.3 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 154.7, 152.6, 149.4, 148.0, 147.7, 144.8, 138.0, 137.0, 135.9 (2C), 126.7, 125.5, 123.7, 119.3, 117.3, 115.5, 113.7, 111.1, 108.4,

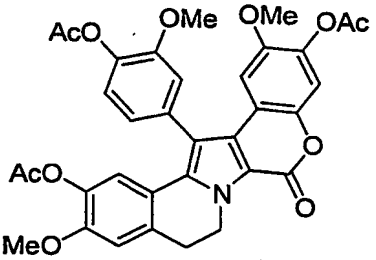
105.756.4, 56.0, 55.8, 55.3, 42.5, 39.1, 38.6, 29.7. MS (ESI) m/z: 694 $(M+23)^+$, 672 $(M+1)^+$. Rf: 0.50 ($CH_2Cl_2$:MeOH, 20:1).

Example 93: Compound **93**



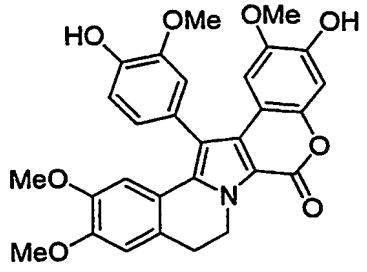

To a solution of **95** (7.0 mg, 0.0135 mmol) and pyridine (4 mL, 0.027 mmol) in $CH_2Cl_2$ (2 mL), hydrocinnamoyl chloride (2 mL, 0.027 mmol) was added under Argon atmosphere and stirred at 23 °C for 24 h. The reaction mixture was washed with saturated aqueous solution of $NaHCO_3$, dried over $Na_2SO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give **93** as a white solid (4.9 mg, 43%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.36-7.22 (m, 9 H), 7.15-7.02 (m, 3H), 6.76 (s, 1H), 6.70 (s, 1H), 6.68 (s, 1H), 4.90-4.74 (m, 2H), 3.90 (s, 3H), 3.75 (s, 3H), 3.40 (s, 3H), 3.38 (s, 3H), 3.16-2.89 (m, 10H). MS (ESI) m/z: 802 $(M+23)^+$, 780 $(M+1)^+$. Rf: 0.38 (hexane:EtOAc, 50:50).

Example 94: Compound **94**



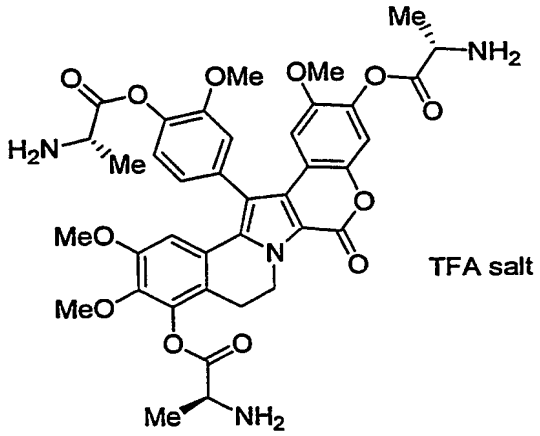

A mixture of **167** (10.0 mg, 0.0193 mmol), $Ac_2O$ (0.75 mL) and pyridine (1.5 mL) was stirred at 23 °C for 18 h under Argon atmosphere. The solvent was evaporated under reduced pressure to give **94** as a brown solid (11.0 mg, 91%.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.20 (d, $J$= 7.8 Hz, 1H), 7.09-7.04 (m, 3H), 6.87 (s, 1H), 6.70 (br s, 2H), 4.92-4.86 (m, 1H), 4.79-4.72 (m, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.43 (s, 3H), 3.17 (t, $J$= 6.3 Hz, 2H), 2.35 (s, 3H), 2.23 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.0, 168.8, 168.5, 155.1, 152.1, 151.1, 147.7, 144.8, 139.9, 138.8, 138.4, 134.9, 133.4, 132.9, 127.2, 123.9, 123.1, 120.3, 120.0, 116.1, 115.4, 114.6, 112.1, 111.9, 105.5, 56.1, 56.0, 55.8, 42.1, 29.2, 20.6 (2C), 20.5. MS (ESI) m/z: 650 $(M+23)^+$, 628 $(M+1)^+$. Rf: 0.28 (hexane:EtOAc, 50:50).

Example 95: Compound **95**



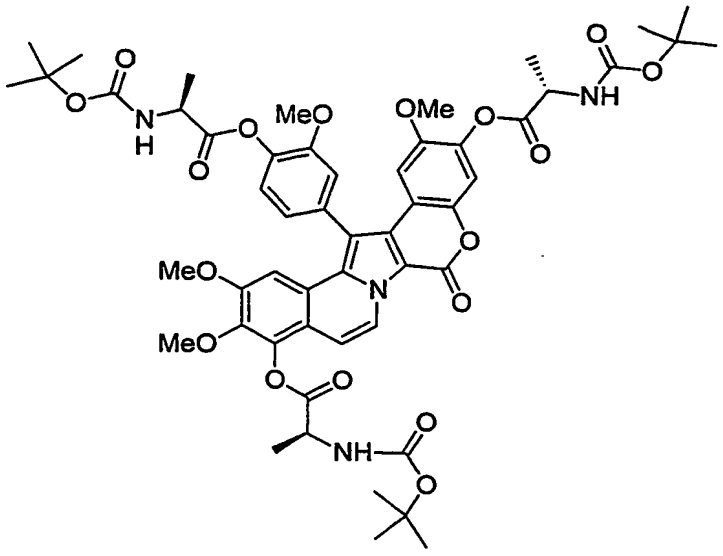

A suspension of **162** (320.6 mg, 0.535 mmol) and $AlCl_3$ (285.1 mg, 2.138 mmol) in anhydrous $CH_2Cl_2$ (15 mL) was stirred from 0 °C to 23 °C for 2 h under Argon atmosphere. MeOH (1 mL) was added and the solvent was evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to afford **95** compound as a yellow solid (170 mg, 61%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.14-7.07 (m, 2H), 6.07-6.96 (m, 2H), 6.76 (s, 1H), 6.71 (s, 1H), 6.64 (s, 1H), 5.75 (s, 1H), 5.72 (s, 1H), 4.98-4.89 (m, 1H), 4.69-4.59 (m, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.50 (s, 3H), 3.38 (s, 3H), 3.15-3.09 (m, 2H). $^{13}C$ NMR (75 MHz, DMSO-$d_6$) $\delta$ 154.3, 148.84, 148.52, 147.0, 146.9, 146.6, 145.7, 144.5, 135.5, 127.7, 126.8, 125.4, 123.4, 119.4, 116.3, 114.7, 112.5, 111.7, 108.7, 105.0, 103.6, 56.0, 55.5, 55.1, 54.5, 42.0, 27.7. MS (ESI) m/z: 516 $(M+1)^+$. Rf: 0.33 ($CH_2Cl_2$:MeOH, 20:1).

Example 96: Compound **96**



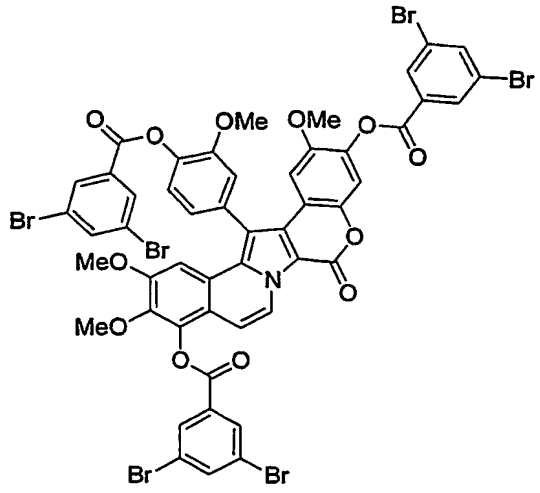

TFA (1 mL) was added to a solution of **46** (12 mg, 0.011 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **96** was obtained as a white solid (12 mg, quant.). The solid was collected by triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.60-7.40 (m, 2H), 7.40-7.20 (m, 2H), 7.00-6.80 (m, 2H), 4.77 (br s, 2H), 4.75-4.40 (m, 3H), 3.86 (s, 3H), 3.80 (s, 3H), 3.44 (s, 3H), 3.42 (s, 3H), 3.05 (br s, 2H), 2.00-1.70 (m, 9H). MS (ESI) m/z: 745 $(M+1)^+$.

Example 97: Compound **97**



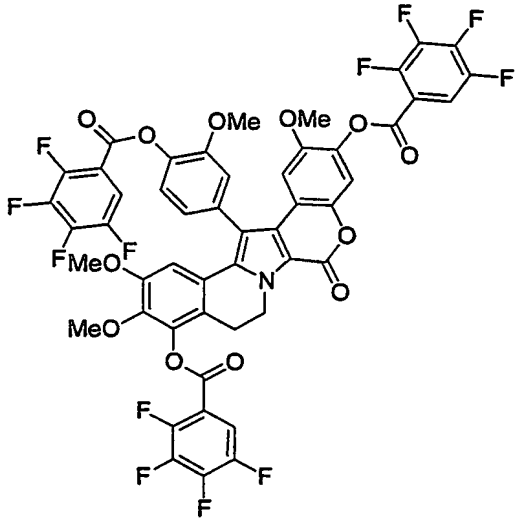
To a solution of **46** (18 mg, 0.017 mmol) in $CHCl_3$ (0.5 mL), DDQ (5.8 mg, 0.025 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 30 h. The reaction was followed by $^1H$ NMR. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel (hexane:EtOAc, 50:50) to give **97** as a yellow solid (16 mg, 88 %). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.23 (d, $J$= 7.6 Hz, 1H), 7.40-7.05 (m, 6H), 6.78 (d, $J$= 8.4 Hz, 1H), 5.20-5.00 (m, 3H), 4.80-4.50 (m, 3H), 3.86 (s, 3H), 3.81 (s, 3H), 3.48 (s, 3H), 3.43 (s, 3H), 1.68 (d, $J$= 7.1 Hz, 3H), 1.62 (d, $J$= 7.2 Hz, 3H), 1.55 (d, $J$=7.1 Hz, 3H), 1.49 (s, 18H), 1.46 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.9, 171.6, 171.3, 155.3, 155.0, 154.9, 153.1, 152.2, 147.6, 145.5, 145.4, 141.6, 140.0, 139.5, 138.8, 134.5, 133.2, 128.3, 128.2, 123.9, 123.6, 123.5, 121.0, 118.3, 115.8, 115.1, 112.1, 109.0, 106.8, 106.2, 104.2, 80.3, 80.1 (2C), 60.8, 56.2, 55.8, 55.6, 49.6, 49.3 (2C), 28.3 (9C), 18.6 (2C), 18.3. MS (ESI) m/z: 1043 $(M)^+$. Rf: 0.42 (hexane:EtOAc, 50:50).

Example 98: Compound **98**



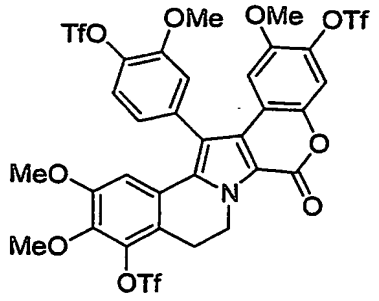
To a solution of **141** (6 mg, 0.0045 mmol) in $CHCl_3$ (0.3 mL), DDQ (1.6 mg, 0.0068 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 18 h. The reaction was followed by $^1H$ NMR. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$) to afford **98** as a white solid (4 mg, 66%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.25 (d, $J$= 7.6 Hz, 1H), 8.39 (d, $J$= 1.8 Hz, 2H), 8.32 (d, $J$= 1.8 Hz, 2H), 8.27 (d, $J$= 1.8 Hz, 2H), 8.01 (t, $J$= 1.8 Hz, 1H), 7.97 (t, $J$= 1.8 Hz, 1H), 7.94 (t, $J$= 1.8 Hz, 1H), 7.43 (d, $J$= 8.0 Hz, 1H), 7.40-7.25 (m, 3H), 7.19 (s, 1H), 7.09 (d, $J$= 7.6 Hz, 1H), 6.91 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.60 (s, 3H), 3.52 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 162.3, 162.1, 162.0, 154.9, 153.3, 152.4, 147.7, 145.5, 141.9, 140.1, 139.5, 139.4, 139.0, 138.8, 134.8, 133.2, 132.2, 132.1, 132.0, 131.9, 131.8, 130.9, 128.8, 128.3, 124.0, 123.7, 123.6, 123.5, 123.3, 123.2, 121.0, 118.1, 116.1, 115.2, 112.2, 109.1, 106.5, 106.3, 104.5, 61.0, 56.3, 55.9, 55.8. MS (ESI) m/z: 1315 $(M)^+$. Rf: 0.73 ($CH_2Cl_2$).

Example 99: Compound **99**



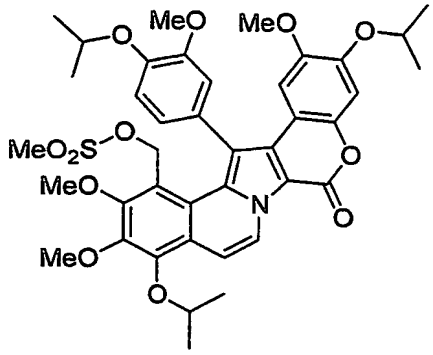
To a solution of **1** (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ (2 mL) 2,3,4,5-tetrafluorobenzoic acid (55 mg, 0.28 mmol), EDC·HCl (54 mg, 0.28 mmol) and DMAP (4 mg, 0.028 mmol) were added and the mixture stirred for 3 h under Argon at 23 °C. $CH_2Cl_2$ (50 mL) was added and then washed with $H_2O$ (2x10 mL) and saturated aqueous solution of $NaHCO_3$ (2x10 mL), dried over anhydrous $Na_2SO_4$, filtered, and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, 200:1) to afford **99** as a white solid (35 mg, 71%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.90-7.70 (m, 3H), 7.38 (d, $J$= 8.0 Hz, 1H), 7.30-7.15 (m, 3H), 6.76 (s, 2H), 5.00-4.80 (br s, 1H), 4.80-4.60 (br s, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.48 (s, 3H), 3.47 (s, 3H), 3.05 (br s, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 159.9, 155.2, 152.3, 152.2, 147.7, 145.2, 141.4, 141.3, 139.7, 138.6, 135.0, 127.2, 124.0, 123.6, 123.0, 119.2, 116.7, 116.0, 115.3, 115.1, 114.2, 113.9, 112.1, 108.3, 105.8, 61.2, 56.6, 56.1, 55.9, 42.1, 22.6. MS (ESI) m/z: 1059 $(M)^+$. Rf: 0.46 ($CH_2Cl_2$).

Example 100: Compound **100**




To a solution of **1** (20 mg, 0.037 mmol) in anhydrous $CH_2Cl_2$ (3 mL) under Argon at 0 °C, triethylamine (0.042 mL, 0.30 mmol), $Tf_2NPh$ (67 mg, 0.188 mmol) and DMAP (1.4 mg, 0.011 mmol) were added and the mixture stirred at 23 °C for 1.5 h. $CH_2Cl_2$ (50 mL) was added and then washed with saturated aqueous solution of $NaHCO_3$ (10 mL) and HCl 1 N (2x10 mL), dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$) to afford **100** as a white solid (30 mg, 85%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.49 (d, $J$= 8.6 Hz, 1H), 7.30-7.20 (m, 3H), 6.63 (s, 1H), 6.62 (s, 1H), 5.00-4.90 (m, 1H), 4.80-4.60 (m, 1H), 3.96 (s, 3H), 3.94 (s, 3H), 3.47 (s, 3H), 3.37 (s, 3H), 3.25-3.15 (m, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.2, 152.7, 152.0, 147.9, 144.4, 141.7, 140.3, 138.7, 137.2, 136.5, 134.1, 126.1, 123.7, 123.4, 122.4, 120.7, 119.3, 117.8, 116.4, 115.4, 112.1, 109.0, 105.7, 61.4, 56.7, 55.8, 55.5, 41.8, 22.6. MS (ESI) m/z: 927 $(M)^+$. Rf: 0.57 ($CH_2Cl_2$).

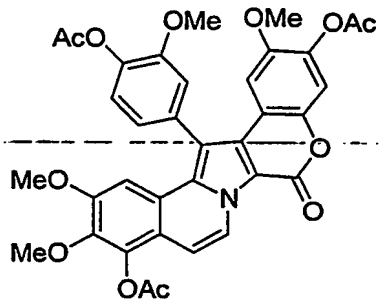
Example 101: Compound **101**




LL-10-Br (15 mg, 0.03 mmol) was added in one portion to a solution of isoquinoline (10 mg, 0.028 mmol) in anhydrous DMA (2 mL) under Argon atmosphere. The solution was stirred at 23 °C for 19 h, then $Et_3N$ (5 µL) was added and the reaction mixture was heated at 80 °C for 20 h. The reaction mixture was cooled to 23 °C, saturated aqueous solution of $NaHCO_3$ (0.2 mL) was added followed by addition of $(KSO_3)_2NO$ (8 mg, 0.03 mmol) and the mixture was stirred at 23 °C for 1 h. Finally, the reaction was quenched with saturated aqueous solution of $NaHCO_3$ and extrated with $CH_2Cl_2$ (4x20 mL). The combined organic phases were dried over $Na_2SO_4$ and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel (hexane:EtOAc, from 3:1 to 1:1) to afford **101**as a white solid (4 mg, 19%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.5 Hz, 1H), 7.38 (d, $J$= 7.5 Hz, 1H), 7.26 (s, 1H), 7.05 (s, 2H), 7.00-6.90 (m, 2H), 4.80-4.50 (m, 3H), 3.95 (s, 5H), 3.85 (s, 3H), 3.75 (s, 3H), 3.54 (s, 2H), 2.92 (s, 3H), 1.50-1.30 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.4, 154.3, 151.0, 147.8, 146.8, 146.6, 146.4, 146.2, 140.7, 140.2,

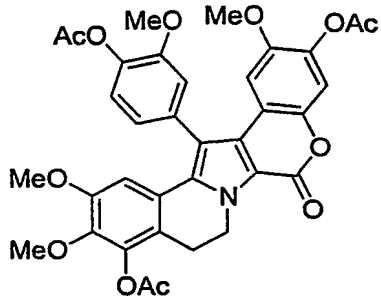
134.7, 128.9, 128.8, 124.3, 124.0, 123.7, 123.1, 120.2, 116.5, 116.2, 115.4, 109.8, 107.7, 105.7, 103.4, 77.2, 71.7, 71.4, 68.6, 61.6, 60.6, 57.6, 56.0, 55.8, 22.8, 22.0, 21.8. MS (ESI) m/z: 722 $(M-^{i}Pr)^{+}$. Rf: 0.50 (hexane:EtOAc, 50:50).

Example 102: Compound **102**




**2** (4.6 mg, 0.0087 mmol) was dissolved in pyridine (1 mL) under Argon and acetic anhydride (0.5 mL) was added in one portion at 23 °C. After stirring at 23 °C overnight, $CH_2Cl_2$ (20 mL) was added and the organic phase washed with HCl 1 N (2x10 mL). After drying over $Na_2SO_4$, the organic solvent was removed under reduced pressure and the resulted residue was subjected to flash chromatography on silica gel (hexane:EtOAc, 50:50) to afford **102** as a white solid (5.4 mg, 96%). $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.24 (d, $J$= 7.6 Hz, 1H), 7.40-7.00 (m, 6H), 6.81 (s, 1H), 3.89 (s, 3H), 3.83 (s, 3H), 3.48 (s, 3H), 3.45 (s, 3H), 2.49 (s, 3H), 2.37 (s, 3H), 2.32 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.8, 168.7, 155.0, 153.2, 152.4, 147.8, 145.5, 141.9, 140.3, 139.8, 139.0, 134.3, 133.3, 128.4, 124.1, 123.6, 123.4, 121.0, 118.2, 115.7, 115.1, 112.2, 112.1, 109.0, 106.6, 106.1, 104.1, 60.8, 56.2, 55.7, 55.6, 20.6 (3C). MS (ESI) m/z: 678 $(M+23)^{+}$. Rf: 0.38 (hexane:EtOAc, 50:50).

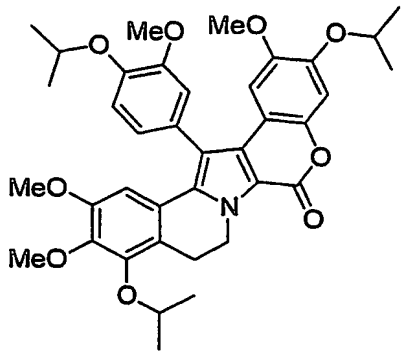
Example 103: Compound **103**




**1** (10 mg, 0.018 mmol) was dissolved in pyridine (2.5 mL) under Argon and acetic anhydride (1.25 mL) was added in one portion at 23 °C. After stirring at 23 °C overnight, $CH_2Cl_2$ (30 mL) was added and the organic phase washed with HCl 1 N (2x10 mL). After drying over $Na_2SO_4$, the organic solvent was removed under reduced pressure and the resulted residue was subjected to flash chromatography on silica gel (hexane:EtOAc, 1:2) to afford **103** as a white solid (12 mg, 99%). $^{1}H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.30-7.05 (m, 4H), 6.68 (s, 2H), 4.95-4.80 (m, 1H), 4.80-4.60 (m, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.42 (s, 3H), 3.38 (s, 3H), 3.00-2.95 (m, 2H), 2.40 (s, 3H), 2.35 (s, 3H), 2.31 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.9, 168.8, 168.7, 155.1, 152.2, 151.8, 147.7, 144.9, 141.6, 141.2, 140.0, 138.9, 134.9, 134.1, 127.2, 123.9, 123.2,

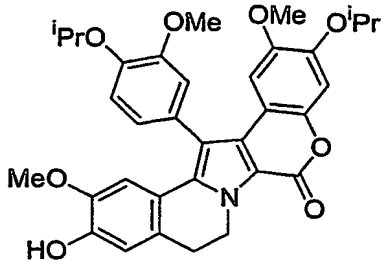
122.6, 119.1, 116.0, 115.8, 114.8, 114.7, 111.9, 107.5, 105.4, 60.8, 56.2, 55.7, 55.4, 41.9, 22.2, 20.6 (2C), 20.5. MS (ESI) m/z: 680 $(M+23)^+$. Rf: 0.32 (hexane:EtOAc, 50:50).

Example 104: Compound 104




LL-10-I (2.30 g, 4.27 mmol) was added in one portion to a solution of isoquinoline (1.20 g, 4.81 mmol) in dry 1,2-dichloroethane (40 mL) under Argon atmosphere. The solution was stirred at 23 °C for 14 h, then diisopropylethylamine (0.75 mL) was added and the reaction mixture was heated at 85 °C for 32 h. The reaction mixture was cooled to 23 °C, silica gel (6.0 g) was added and the solvent was evaporated under reduced pressure. The resulted residue was subjected to flash chromatography on silica gel (hexane:$CH_2Cl_2$:$Et_2O$, from 5:5:1 to 5:5:2) to afford 104 as a white solid (1.58 g, 56%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.15-7.00 (m, 3H), 6.91 (s, 1H), 6.63 (s, 1H), 6.59 (s, 1H), 4.73 (t, $J$= 7.0 Hz, 2H), 4.65-4.50 (m, 3H), 3.82 (s, 6H), 3.41 (s, 3H), 3.33 (s, 3H), 3.14 (t, $J$= 6.8 Hz, 2H), 1.39 (t, $J$= 6.3 Hz, 12H), 1.31 (d, $J$= 6.1 Hz, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.6, 151.7, 151.3, 148.6, 147.0, 146.9, 146.5, 145.9, 142.5, 135.5, 128.6, 128.1, 123.4, 123.0, 121.1, 116.9, 115.6, 114.6, 113.8, 110.3, 104.9, 104.8, 103.5, 75.7, 71.8, 71.4, 60.5, 56.2, 55.4, 55.1, 42.3, 22.7, 21.9, 21.8. MS (ESI) m/z: 658 $(M+1)^+$. Rf: 0.56 (hexane:EtOAc, 50:50).

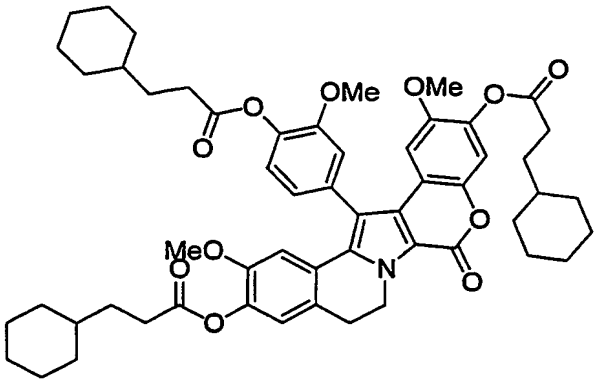
Example 105: Compound 105




A solution of 163 (21 mg, 0.031 mmol) and Pd/C (3.2 mg) in MeOH (5 mL) was placed under vacuum and purged with Argon. The vacuum/Argon cycles was repeated three times. The solution was placed under vacuum and filled with $H_2$. The reaction mixture was stirred under an atmosphere of $H_2$ at 50 psi for 22 h at 23 °C in a Parr apparatus. The reaction mixture was filtered through a pad of Celite, washed with MeOH and the solvent removed under vacuum. The resulted residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to afford 105 (10 mg, 56%). $^1H$ NMR (300 MHz,

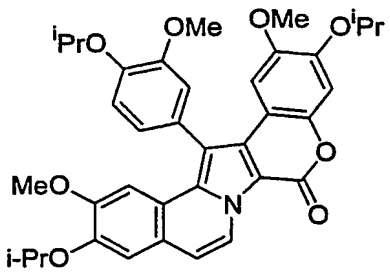
$CDCl_3$) $\delta$ 7.12-7.03 (m, 3H), 6.92 (s, 1H), 6.81 (s, 1H), 6.69 (s, 1H), 6.67 (s, 1H), 4.85-4.69 (m, 2H), 4.64-4.40 (m, 2H), 3.82 (s, 3H), 3.43 (s, 3H), 3.39 (s, 3H), 3.08 (t, $J$= 6.6 Hz, 2H), 1.42-1.37 (m, 12H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.6, 151.3, 147.0, 146.9, 146.5, 146.0, 145.8, 145.1, 136.0, 129.3, 128.7, 128.2, 127.5, 125.0, 123.4, 119.7, 116.9, 114.6, 114.2, 110.4, 108.3, 104.9, 103.5, 71.8, 71.4, 56.2, 55.5, 55.3, 42.4, 28.5, 21.9 (2C), 21.8 (2C). MS (ESI) m/z: 608 $(M+23)^+$, 586 $(M+1)^+$. Rf: 0.30 (hexane:EtOAc, 50:50).

Example 106: Compound **106**



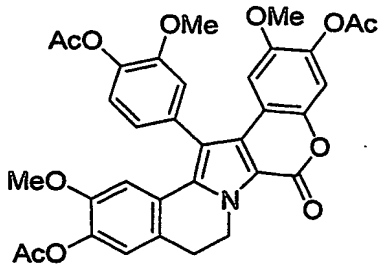

A suspension of **109** (25 mg, 0.05 mmol), cyclohexanepropionic acid (31 mg, 0.20 mmol), EDC·HCl (38 mg, 0.20 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 3 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL) and both aqueous phases were extracted with $CH_2Cl_2$ (10 mL). The combined organic layers were dried over $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 100:1 to 50:1) to give **106** as a white solid (33 mg, 72%).$^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.20 (d, $J$= 7.9 Hz, 1H), 7.14-7.07 (m, 3H), 6.94 (s, 1H), 6.79 (s, 1H), 6.70 (s, 1H), 4.92-4.84 (m, 1H), 4.79-4.70 (m, 1H), 3.80 (s, 3H), 3.42 (s, 3H), 3.35 (s, 3H), 3.11 (t, $J$= 6.7 Hz, 2H), 2.64-2.54 (m, 6H), 1.81-1.60 (m, 21H), 1.39-1.12 (m, 12H), 0.98-0.91 (m, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 172.1, 171.9, 171.8, 155.1, 152.3, 149.9, 147.7, 144.9, 140.1, 139.5, 139.0, 135.1, 133.8, 127.1, 125.9, 125.5, 123.9, 123.1, 122.6, 115.9 (2C), 114.8, 114.6, 111.9, 109.7, 105.4, 56.2, 55.7, 55.5, 42.4, 37.2 (3C), 37.1 (3C), 32.9 (6C), 32.2 (3C), 31.6 (3C), 28.0, 26.5 (3C), 26.2 (3C). MS (ESI) m/z: 916 $(M+1)^+$. Rf: 0.17 (hexane:EtOAc, 4:1).

Example 107: Compound **107**



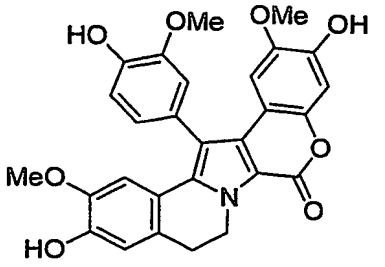
A suspension of **110** (301 mg, 0.480 mmol) and DDQ (139 mg, 0.611 mmol) in $CHCl_3$ (10 mL) was refluxed for 2 h. The mixture was cooled at 23 °C then filtered through Celite, and washed with $CH_2Cl_2$. The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give **107** (283 mg, 94%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.24 (d, $J$= 7.3 Hz, 1H), 7.29-7.17 (m, 2H), 7.12-7.10 (m, 2H), 7.04-7.02 (m, 2H), 6.98 (s, 1H), 6.76 (s, 1H), 4.70-4.56 (m, 3H), 3.84 (s, 3H), 3.44 (s, 3H), 3.43 (s, 3H), 1.44-1.39 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.3, 151.2, 150.0, 148.3, 147.7, 147.0, 146.4, 146.3, 134.2, 129.2, 128.6, 124.6, 123.8, 122.9, 118.8, 116.7, 114.9, 112.1, 110.8, 110.2, 109.8, 107.6, 105.5, 105.3, 103.2, 71.6, 71.3, 71.0, 56.0, 55.3, 55.0, 21.8 (3C), 21.7, 21.7, 21. MS (ESI) m/z: 648 $(M+23)^+$, 626 $(M+1)^+$. Rf: 0.35 (hexane:EtOAc, 2:1).

Example 108: Compound **108**




A solution of **109** (40 mg, 0.08 mmol) and acetic anhydride (0.5 mL, 5.289 mmol) in pyridine (1 mL) was stirred at 23 °C under Argon atmosphere for 4 h. The resulting pale yellow solution was washed with HCl 1 N (2x10 mL). The organic phase was dried over $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 40:1) to give **108** as a white solid (38 mg, 76%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.22 (d, $J$= 7.9 Hz, 1H), 7.15-7.09 (m, 3H), 6.95 (s, 1H), 6.79 (s, 1H), 6.69 (s, 1H), 4.92-4.71 (m, 2H), 3.81 (s, 3H), 3.43 (s, 3H), 3.35 (s, 3H), 3.12 (t, $J$= 6.7 Hz, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 2.30 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 169.0, 168.8, 168.6, 155.1, 152.2, 149.9, 147.7, 144.9, 140.0, 139.4, 138.9, 135.0, 134.0, 127.1, 125.9, 125.7, 123.9, 123.2, 122.6, 116.0, 115.9, 114.9, 114.6, 112.0, 109.7, 105.4, 56.2, 55.7, 55.5, 42.5, 28.1, 20.6 (3C). MS (ESI) m/z: 628 $(M+1)^+$. Rf: 0.32 ($CH_2Cl_2$:MeOH, 100:1).

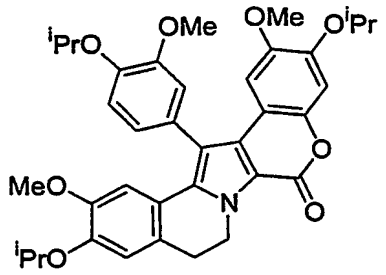
Example 109: Compound **109**




A suspension of **110** (1.422 g, 2.265 mmol) and $AlCl_3$ (1.208 g, 9.061 mmol) in anhydrous $CH_2Cl_2$ (43 mL) was stirred at 23 °C for 2.5 h under Argon atmosphere. MeOH (20 mL) was added and the solvent evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 20:1

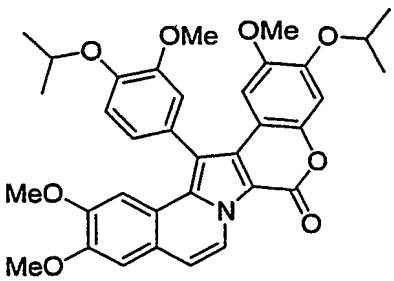
to 10:1 to 5:1) to afford **109** as a pale brown solid (1.11 g, 97%). $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.64 (s, 1H), 9.41 (s, 1H), 9.24 (s, 1H), 7.01 (s, 1H), 6.99 (d, $J$= 8.1 Hz, 1H), 6.88 (d, $J$= 8.4 Hz, 1H), 6.78 (s, 1H), 6.73 (s, 1H), 6.67 (s, 1H), 6.59 (s, 1H), 4.58 (t, $J$= 6.5 Hz, 2H), 3.73 (s, 3H), 3.34 (s, 3H), 3.25 (s, 3H), 2.99 (t, $J$= 6.4 Hz, 2H). $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 154.3, 148.5, 147.1, 146.9, 146.5, 146.0, 145.7, 144.4, 135.9, 127.7, 127.1, 125.5, 123.4, 118.1, 116.3, 115.3, 114.7, 114.3, 112.2, 109.2, 108.8, 105.1, 103.6, 56.0, 55.0, 54.7, 42.0, 27.5. MS (ESI) m/z: 524 $(M+23)^+$. Rf: 0.55 ($CH_2Cl_2$:MeOH 10:1).

Example 110: Compound **110**




6-Isopropoxy-7-methoxy-3,4-dihydroisoquinoline (1.06 g, 4.83 mmol) was added to a solution of iodoacetic acid 5-isopropoxy-2-(4-isopropoxy-3-methoxyphenylethynyl)-4-methoxyphenyl ester (LL10-I) (2.30 g, 4.27 mmol) in dry 1,2-dichloroethane (distilled over $CaH_2$, 40 mL) under Argon atmosphere. The reaction mixture was stirred for 8 h at 23 °C turning to an orange solution. At this time, DIPEA (0.750 mL, 4.31 mmol) was added and the resulting brown solution stirred at 85 °C for 32 h. The reaction mixture was cooled to 23 °C, silica gel (6 g) was added and the solvent removed under reduced pressure. The resulting crude was purified by chromatography on silica gel (hexane:$CH_2Cl_2$:$Et_2O$, 5:5:2) to afford **110** as a pale yellow solid (1.27 g, 47%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.08-7.04 (m, 3H), 6.92 (s, 1H), 6.76-6.74 (m, 2H), 6.67 (s, 1H), 4.87-4.71 (m, 2H), 4.65-4.48 (m, 3H), 3.82 (s, 3H), 3.42 (s, 3H), 3.33 (s, 3H), 3.09 (t, $J$= 6.6 Hz, 2H), 1.41-1.36 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 155.5, 151.2, 148.5, 147.2, 146.9, 146.8, 146.4, 145.8, 135.9, 128.5, 128.1, 126.3, 123.3, 120.1, 116.8, 114.8, 114.6, 114.5, 113.6, 110.3, 109.1, 104.8, 103.4, 71.7, 71.3, 71.2, 56.1, 55.4, 55.0, 42.3, 28.5, 22.0 (2C), 21.8, 21.8, 21.7 (2C). MS (ESI) m/z: 628 $(M+1)^+$. Rf: 0.28 (Hex:$CH_2Cl_2$:$Et_2O$, 5:5:2).

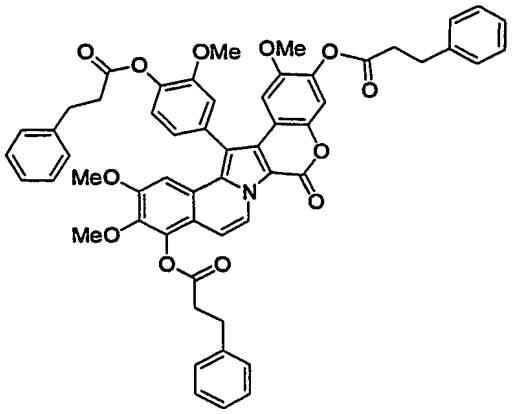
Example 111: Compound **111**




A supension of **69** (188.0 mg, 0.3135 mmol) and DDQ (89.0 mg, 0.3919 mmol) in $CHCl_3$ (5 mL) was refluxed under Argon atmosphere for 3 h. The reaction mixture was

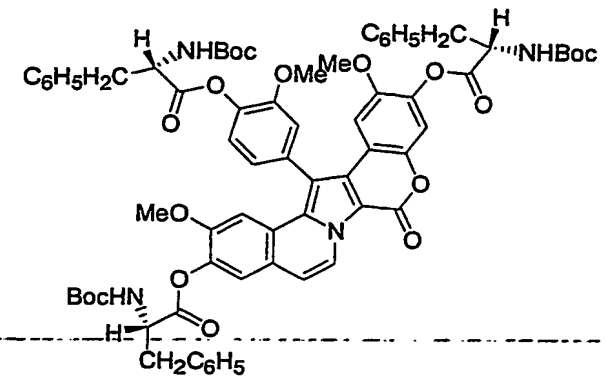
cooled to 23 °C, filtered throught Celite, washed with $CH_2Cl_2$ (10 mL) and the filtrate was concentrated under resuded pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give **111** as a white solid (176.3 mg, 94 %). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.25 (d, $J$= 7.3 Hz, 1H), 7.19-7.04 (m, 6H), 6.97 (s, 1H), 6.76 (s, 1H), 4.66-4.56 (m, 2H), 3.99 (s, 3H), 3.84 (s, 3H), 3.47 (s, 3H), 3.45 (s, 3H), 1.44-1.40 (m, 12H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.5, 151.3, 150.0, 149.1, 147.8, 147.1, 146.6, 146.5, 134.3, 129.4, 128.6, 124.7, 123.9, 123.3, 119.1, 116.8, 115.0, 112.2, 111.0, 109.9, 107.8, 107.3, 105.4, 105.3, 103.4, 71.7, 71.4, 56.1, 55.9, 55.9, 55.4, 55.10, 21.9, 21.8. MS (ESI) m/z: 598 $(M+1)^+$. Rf: 0.50 (hexane:EtOAc, 50:50).

Example 112: Compound **112**



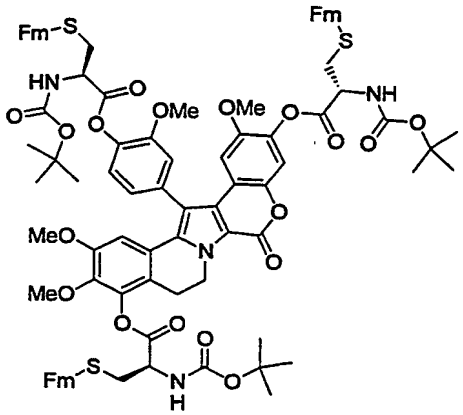

A suspension of **116** (18 mg, 0.019 mmol) and DDQ (9 mg, 0.038 mmol) in $CHCl_3$ (2 mL) was refluxed for 23 h. The mixture was cooled to 23 °C then filtered through Celite, and washed with $CH_2Cl2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, from 2:1 to 1:1) to give **112** (17 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.11 (d, $J$= 7.5 Hz, 1H), 7.50-7.00 (m, 20H), 6.78 (s, 1H), 6.71 (d, $J$= 7.5 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.47 (s, 3H), 3.40 (s, 3H), 3.20-2.80 (m, 12H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.8, 170.7, 155.0, 153.1, 152.3, 147.7, 145.4, 141.8, 140.2, 140.1, 140.0, 139.9, 139.7, 138.9, 134.2, 133.2, 128.7, 128.6, 128.5, 128.4, 128.3, 126.7, 126.5, 126.4, 124.0, 123.3, 123.2, 120.9, 118.2, 115.6, 115.0, 112.1, 108.9, 106.5, 106.1, 104.1, 60.8, 56.2, 55.7, 55.6, 35.5(3C), 31.0, 30.9, 30.8. MS (ESI) m/z: 948 $(M+23)^+$, 926$(M+1)^+$. Rf: 0.39 (hexane:EtOAc, 2:1).

Example 113: Compound **113**



A suspension of **121** (50 mg, 0.040 mmol) and DDQ (18 mg, 0.080 mmol) in $CHCl_3$ (2 mL) was refluxed for 22 h. The mixture was cooled to 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 80:1) to give **113** (43 mg, 86%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.3 Hz, 1H), 7.37-7.20 (m, 20H), 7.08-7.03 (m, 2H), 6.80 (d, $J$= 2.2 Hz, 1H), 5.29-5.02 (m, 3H), 4.90-4.88 (m, 3H), 3.85 (s, 3H), 3.44 (s, 6H), 3.41-3.23 (m, 6H), 1.46 (s, 9H), 1.43 (s, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.1, 170.0, 169.9, 155.1 (2C), 154.9, 152.3, 150.9, 147.6, 145.3, 140.5, 139.9, 139.3, 135.8 (2C), 134.5, 133.4, 125.0 (9C), 128.6 (6C), 128.1, 128.0, 127.1 (2C), 124.0, 123.7, 123.6, 123.1, 120.7, 115.8, 115.1, 112.8, 112.3, 112.1, 109.1, 106.4, 106.1, 80.1 (3C), 56.2 (2C), 55.7, 55.6, 55.5, 54.4, 38.1 (3C), 28.2 (9C). MS (ESI) m/z: 1263 $(M+23)^+$, 1241 $(M+1)^+$. Rf: 0.56 ($CH_2Cl_2$:MeOH, 50:1).

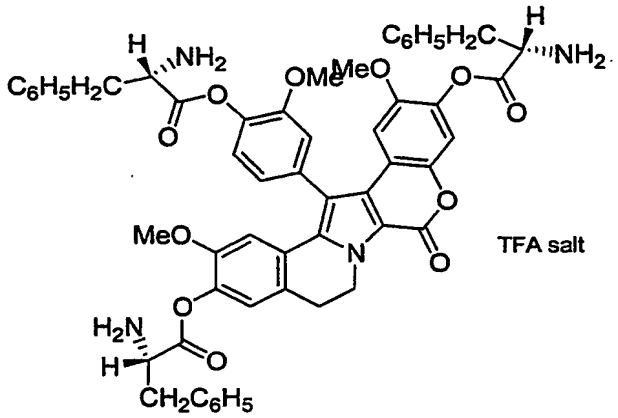
Example 114: Compound **114**



A suspension of **1** (50 mg, 0.094 mmol), (L)-N-Boc-Cys(Fm) (225 mg, 0.56 mmol), EDC·HCl (108 mg, 0.56 mmol) and DMAP (7 mg, 0.056 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 3 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with $H_2O$ (2x20 mL) and saturated aqueous solution of $NaHCO_3$ (2x20 mL), dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 50:50) to give **114** as a white solid (140 mg, 88%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.85-7.65 (m, 12H), 7.45-7.25 (m, 12H), 7.25-7.05 (m, 4H), 6.64 (t, $J$ = 2.9 Hz, 2H), 5.50-5.30 (m, 3H), 4.90-4.70 (m, 4H), 4.60 (br s, 1H), 4.25-4.10 (m, 3H),

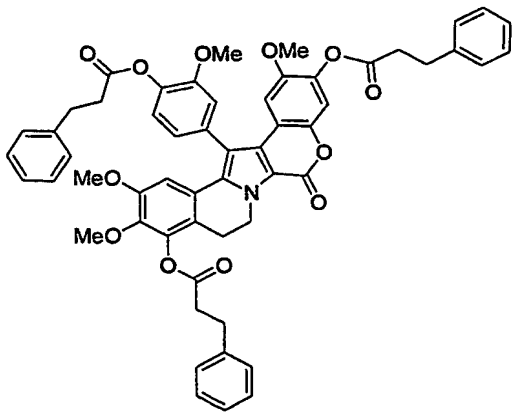
3.75 (s, 3H), 3.72 (s, 3H), 3.35 (s, 3H), 3.33 (s, 3H), 3.30-3.10 (m, 12H), 2.95 (m, 2H), 1.48 (s, 18H), 1.46 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.3, 169.1, 155.1, 154.9, 151.9, 151.7, 147.4, 145.7, 145.5, 144.8, 141.1, 141.0, 140.9, 139.5, 138.4, 134.7, 134.4, 127.7, 127.6, 127.5, 127.0, 126.9, 124.8, 124.7, 124.6, 123.7, 123.2, 122.6, 120.0, 119.9, 119.8, 119.3, 116.2, 115.6, 114.8, 114.7, 111.9, 107.7, 105.4, 80.5, 80.4, 80.3, 60.8, 56.1, 55.6, 55.5, 53.6, 53.4, 46.9, 41.9, 37.3, 37.2, 37.1, 35.6, 35.2, 31.9, 29.6, 28.3, 22.2. MS (ESI) m/z: 1698 $(M+23)^+$, 1676 $(M+1)^+$. Rf: 0.19 (hexane:EtOAc, 2:1).

Example 115: Compound **115**



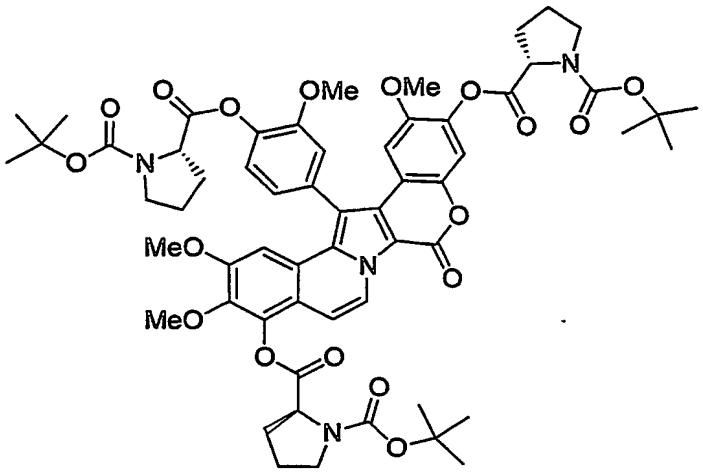

TFA (1 mL) was added to a solution of **121** (15 mg, 0.012 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred to 23 °C for 2.5 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **115** as a white solid (17 mg, quant.). $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.44-7.35 (m, 17H), 7.26 (d, $J$= 8.1 Hz, 1H), 7.10 (d, $J$= 1.6 Hz, 1H), 7.06 (s, 1H), 6.88 (d, $J$= 3.5 Hz, 1H), 6.78 (d, $J$= 3.5 Hz, 1H), 4.79-4.70 (m, 3H), 4.63 (t, $J$= 6.7 Hz, 2H), 3.89 (s, 3H), 3.53-3.26 (m, 6H), 3.44 (s, 3H), 3.36 (s, 3H), 3.16 (t, $J$= 6.7 Hz, 2H). MS (ESI) m/z: 965 $(M+23)^+$, 943 $(M+1)^+$.

Example 116: Compound **116**



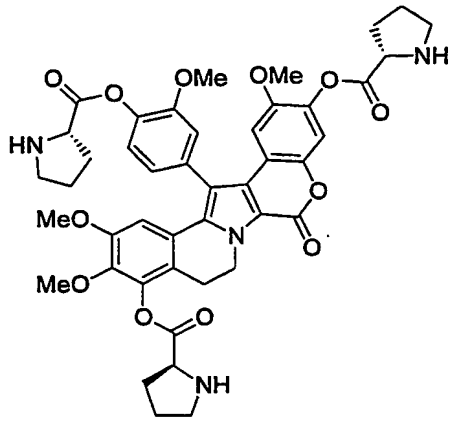
To a solution of 2 (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ and pyridine (23 μL, 0.28 mmol), and hydrocinnamoyl chloride (42 μL, 0.28 mmol) was added at 23 °C and the mixture stirred under Argon atmosphere for 2 h. The mixture was quenched wtih $H_2O$, the residue was extracted with EtOAc, washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (2x10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel (hexane:EtOAc, from 2:1 to 1:1) to give 116 as a white solid (32 mg, 74%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.40-7.20 (m, 15H), 7.15-7.05 (m, 3H), 7.02 (s, 1H), 6.66 (s, 2H), 4.80-4.70 (m, 1H), 4.70-4.50 (m, 1H), 3.78 (s, 3H), 3.73-(s, 3H), 3.39 (s, 3H), 3.38 (s, 3H), 3.20-2.80 (m, 12H), 2.71-(t, $J$= 6.4 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.8, 170.7, 170.6, 155.0, 152.2, 151.8, 147.6, 144.9, 141.5, 141.1, 140.2, 140.1, 140.0, 139.9, 138.9, 134.8, 134.0, 128.6, 128.5, 128.4, 128.3, 128.3, 128.2, 127.1, 126.6, 126.4, 126.3, 123.8, 123.2, 122.5, 119.1, 115.9, 115.7, 114.7, 114.6, 111.8, 107.5, 105.4, 60.7, 56.2, 55.7, 55.5, 41.8, 35.5, 35.4, 35,3 30.9, 30.8, 30.8, 21.9. MS (ESI) m/z: 950 $(M+23)^+$, 928 $(M+1)^+$. Rf: 0.37 (hexane:EtOAc, 2:1).

Example 117: Compound 117



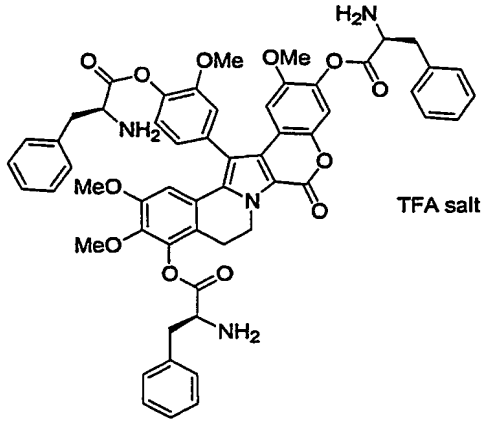
To a solution of 124 (60 mg, 0.053 mmol) in $CHCl_3$ (2 mL), DDQ (24 mg, 0.10 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 31 h. The reaction was followed by $^1H$ NMR. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 30:1) to give 117 as a brownish solid (40 mg, 67%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.21 (d, $J$= 7.3 Hz, 1H), 7.50-7.00 (m, 6H), 6.85-6.70 (m, 1H), 4.80-4,40 (m, 3H), 3.86 (s, 3H), 3.80 (s, 3H), 3.75-3.50 (m, 6H), 3.47 (s, 3H), 3.42 (s, 3H), 2.50-2.20 (m, 6H), 2.20-1.85 (m, 6H), 1.52 (s, 9H), 1.49 (s, 9H), 1.47 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.5, 170.9, 170.8, 155.0, 154.6, 154.4, 154.3, 153.8, 153.7, 152.4, 147.7, 145.5, 141.6, 140.1, 139.7, 134.4, 133.2, 124.2, 123.6, 123.4, 123.2, 121.0, 118.7, 115.7, 115.2, 112.3, 111.9, 107.5, 106.6, 106.1, 104.1, 80.2, 80.1, 79.9, 60.7, 59.0, 58.9, 56.1, 55.8, 55.7, 55.5, 46.6, 46.5, 46.4, 28.5, 28.4, 28.2, 24.5, 24.4, 24.3, 23.6, 23.5, 23.4. MS (ESI) m/z: 1143 $(M+23)^+$. Rf: 0.32 ($CH_2Cl_2$:MeOH, 50:1).

Example 118: Compound 118



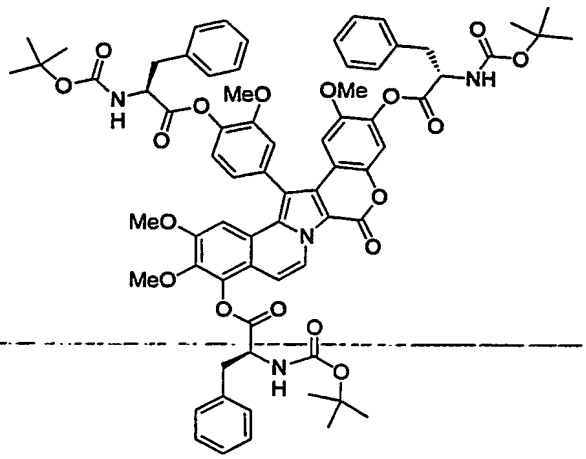
TFA (1 mL) was added to a solution of **124** (25 mg, 0.022 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **118** was obtained as a white solid (25 mg, quant.). The solid was collected by triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.49 (d, $J$= 7.8 Hz, 1H), 7.41 (s, 1H), 7.30-7.20 (m, 2H), 6.81 (d, $J$= 7.9 Hz, 1H), 6.76 (d, $J$= 9.7 Hz, 1H), 4.90-4.70 (m, 5H), 3.87 (s, 3H), 3.81 (s, 3H), 3.60-3.40 (m, 12H), 3.08 (br t, 2H), 2.70-2.30 (m, 6H), 2.30-2.00 (m, 6H). MS (ESI) m/z: 823 $(M+1)^+$.

Example 119: Compound **119**



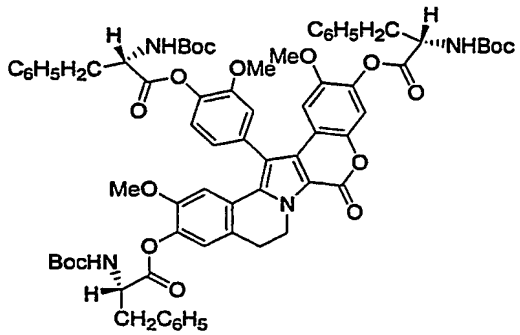

TFA (1 mL) was added to a solution of **125** (28 mg, 0.022 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **119** was obtained as a white solid (28 mg, 99%). The solid was collected by triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.50-7.35 (m, 16H), 7.30-7.20 (m, 2H), 7.15-7.10 (m, 1H), 6.82-6.75 (m, 2H), 4.85-4.55 (m, 5H), 3.88 (s, 3H), 3.81 (s, 3H), 3.60-3.40 (m, 12H), 2.94 (br s, 2H). MS (ESI) m/z: 973 $(M)^+$.

Example 120: Compound **120**



To a solution of **125** (67 mg, 0.052 mmol) in $CHCl_3$ (2 mL), DDQ (24 mg, 0.10 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 31 h. The reaction was followed by $^1H$ NMR. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, 50:1) to give **120** as a yellow solid (54 mg, 80 %). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.12 (dd, $J$= 7.5, 2.5 Hz, 1H), 7.40-7.20 (m, 19H), 7.10-7.00 (m, 2H), 6.79 (d, $J$= 4.0 Hz, 1H), 5.20-4.80 (m, 6H), 3.86 (s, 3H), 3.85 (s, 3H), 3.48 (s, 3H), 3.44 (s, 3H), 3.40-3.20 (m, 6H), 1.46 (s, 18H), 1.43 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.6, 170.0, 169.8, 155.3, 155.1, 155.0, 154.8, 153.1, 152.2, 147.5, 145.3 (2C), 141.7, 139.8, 139.2 (2C), 138.8, 135.8, 135.7, 135.6, 134.6, 133.1 (2C), 129.5 (3C), 129.4 (3C), 128.8 (2C), 128.6 (2C), 128.1, 127.3, 127.2, 123.9, 123.6, 123.3, 120.9, 118.2, 115.8, 115.1, 112.0, 108.9, 106.9, 106.1, 104.2, 80.4, 80.2, 80.0, 60.8, 56.2, 56.1, 55.7, 54.7, 54.3 (2C), 38.1 (2C), 37.8, 28.2 (9C). MS (ESI) m/z: 1293 $(M+23)^+$. Rf: 0.32 ($CH_2Cl_2$:MeOH, 60:1).

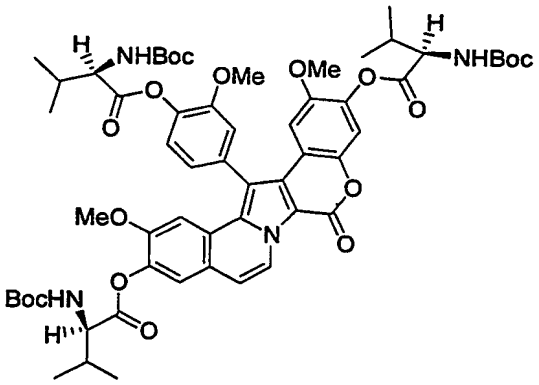
Example 121: Compound **121**



A suspension of **109** (50 mg, 0.0997 mmol), Boc-L-Phe-OH (106 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 6 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL) and both aqueous phases were extracted with $CH_2Cl_2$ (10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 100:1) to give **121** as a white solid (87 mg, 68%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.34-7.26 (m,

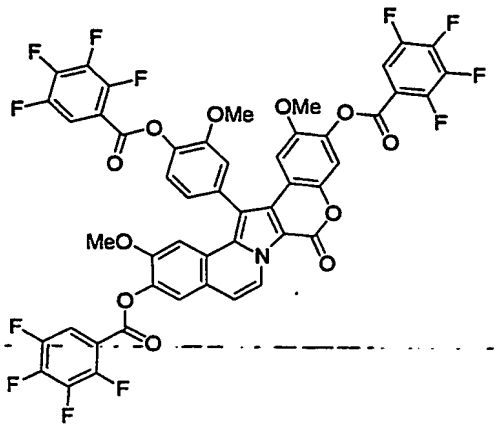
15H), 7.16 (bs, 2H), 7.10 (s, 1H), 7.05 (s, 1H), 6.91 (s, 1H), 6.78-6.68 (m, 2H), 4.99 (t, $J$= 8.6 Hz, 2H), 4.88-4.72 (m, 6H), 3.81 (s, 3H), 3.41 (s, 3H), 3.34 (s, 3H), 3.30-3.12 (m, 8H), 1.44 (s, 9H), 1.43 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.1, 169.9 (2C), 155.0, 154.9, 152.0, 149.7, 147.5, 144.7, 139.6, 139.0, 138.4, 135.8 (2C), 134.8, 134.2, 129.4 (9C), 129.2, 128.5 (6C), 127.1 (2C), 126.9, 125.9, 125.7, 123.8, 123.1, 122.5, 116.1, 115.8, 114.9, 114.7, 111.8, 109.7, 105.4, 80.0 (3C), 56.1, 55.6, 55.4, 54.3 (3C), 42.3, 38.0 (3C), 28.2 (9C), 27.9. MS (ESI) m/z: 1265 $(M+23)^+$. Rf: 0.65 ($CH_2Cl_2$:MeOH, 30:1).

Example 122: Compound **122**



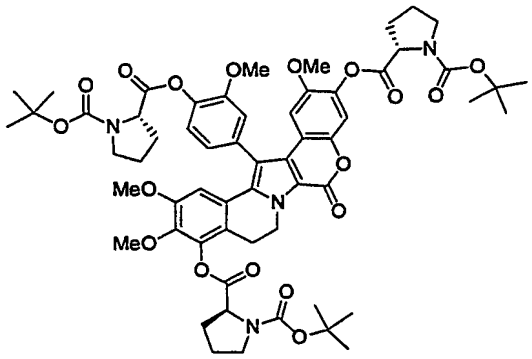

A suspension of **144** (50 mg, 0.045 mmol) and DDQ (21 mg, 0.091 mmol) in $CHCl_3$ (2 mL) was refluxed for 22 h. The mixture was cooled at 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 50:1) to give **122** (47 mg, 94%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.26 (d, $J$= 7.3 Hz, 1H), 7.42 (s, 1H), 7.31-7.26 (m, 2H), 7.23-7.18 (m, 3H), 7.09 (d, $J$= 7.5 Hz, 1H), 6.80 (d, $J$= 7.5 Hz, 1H), 5.09-5.06 (m, 3H), 4.57-4.50 (m, 3H), 3.80 (s, 3H), 3.43 (s, 6H), 2.45-2.34 (m, 3H), 1.50 (s, 9H), 1.47 (s, 18H), 1.14-1.00 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.4 (b), 155.7, 154.9, 152.3, 150.9, 147.6, 145.4, 140.6, 140.0, 139.4, 134.5, 133.4, 128.1, 124.0, 123.8, 123.6, 123.1, 120.8, 115.8, 115.1, 112.8, 112.2, 112.2, 109.1, 106.4, 106.1, 80.0 (3C), 58.5 (2C), 56.0, 55.6, 55.5, 55.4, 30.0 (3C), 28.3 (9C), 19.2, 19.1 (2C), 17.2, 17.1 (2C). MS (ESI) m/z: 1119 $(M+23)^+$, 1097 $(M+1)^+$. Rf: 0.33 ($CH_2Cl_2$:MeOH, 100:1).

Example 123: Compound **123**



A suspension of **139** (20 mg, 0.019 mmol) and DDQ (9 mg, 0.039 mmol) in $CCl_4$ (2 mL) was refluxed for 7 h. The mixture was cooled at 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 100:1) to give **123** (15 mg, 75%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.24 (d, $J$= 7.5 Hz, 1H), 7.84-7.75 (m, 3H), 7.54 (s, 1H), 7.45 (d, $J$= 8.4 Hz, 1H), 7.37-7.35 (m, 2H), 7.30 (s, 1H), 7.26 (s, 1H), 7.08 (d, $J$= 7.3 Hz, 1H), 6.90 (s, 1H), 3.87 (s, 3H), 3.52 (s, 3H), 3.52 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 159.7 (3C), 154.8, 152.3, 150.8, 148.2, 147.6, 145.4, 140.3, 139.8, 139.2, 135.0, 133.4, 128.0, 124.0, 123.9, 123.8, 123.7, 123.2, 120.7, 116.2, 115.3, 113.8, 113.6, 112.8, 112.4, 112.1, 109.2, 106.6, 106.3, 56.4, 55.9, 55.8. MS (ESI) m/z: 1050 $(M+23)^+$, 1028 $(M+1)^+$. Rf: 0.63 ($CH_2Cl_2$).

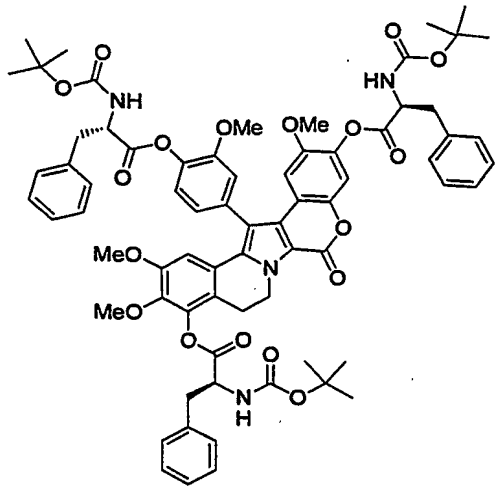
Example 124: Compound **124**



A suspension of **1** (50 mg, 0.094 mmol), (L)-N-Boc-Pro (121 mg, 0.56 mmol), EDC·HCl (108 mg, 0.56 mmol) and DMAP (7 mg, 0.056 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 3 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with $H_2O$ (2x20 mL) and saturated aqueous solution of $NaHCO_3$ (2x20 mL), dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 20:1) to give **124** as a white solid (105 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.20-7.10 (m, 2H), 7.10-7.00 (m, 2H), 6.70-6.60 (m, 2H), 4.90 (br s, 1H), 4.70-4.40 (m, 4H), 3.78 (s, 6H), 3.70-3.40 (m, 6H), 3.39 (s, 3H), 3.36 (s, 3H), 3.20-2.95 (m, 2H), 2.50-2.20 (m, 6H), 2.15-1.85 (m, 6H), 1.48 (s, 18H), 1.46 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.3, 170.9, 170.7, 155.0, 154.4, 153.8, 152.2, 151.7, 147.6, 144.8, 141.4, 141.0, 139.8, 138.7, 134.3, 127.1, 124.0, 123.4, 123.2,

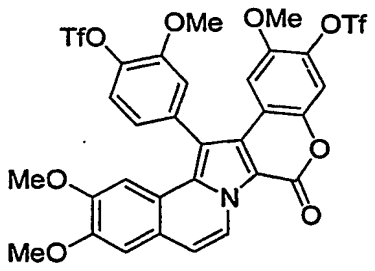
122.6, 119.9, 119.0, 116.0, 115.7, 114.7, 112.1, 111.6, 107.5, 105.4, 80.2, 80.0, 79.9, 60.6, 58.9, 58.8, 56.1, 55.7, 55.6, 55.5, 46.6, 46.5, 46.4, 42.0, 28.3, 24.4, 24.3, 23.6, 23.5, 23.4, 23.3, 22.0. MS (ESI) m/z: 1145 $(M+23)^+$, 1124 $(M+1)^+$. Rf: 0.64 ($CH_2Cl_2$:MeOH, 20:1).

Example 125: Compound **125**



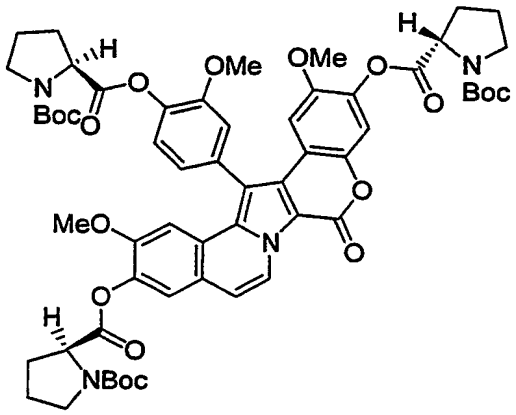

A suspension of **1** (50 mg, 0.094 mmol), (L)-N-Boc-Phe (150 mg, 0.56 mmol), EDC·HCl (108 mg, 0.56 mmol) and DMAP (7 mg, 0.056 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 3 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with $H_2O$ (2x20 mL) and saturated aqueous solution of $NaHCO_3$ (2x20 mL), dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 30:1) to give **125** as a brown solid (119 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.50-7.25 (m, 15H), 7.20-7.10 (m, 3H), 7.03 (s, 1H), 5.10-5.00 (m, 3H), 5.00-4.80 (m, 3H), 4.75-4.50 (m, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 3.78 (s, 6H), 3.40 (s, 3H), 3.37 (s, 3H), 3.35-3.00 (m, 6H), 2.95-2.85 (m, 2H), 1.44 (s, 9H), 1.43 (s, 9H), 1.42 (s, 9H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.4, 169.9 (2C), 155.2, 154.9, 152.1, 151.8, 147.5, 144.8, 141.3, 141.0, 139.6, 138.4, 135.8, 135.6, 134.7, 134.3, 129.5 (3C), 129.4 (2C), 129.2 (2C), 128.7 (2C), 128.5 (2C), 128.4 (2C), 127.2, 127.1, 126.9, 123.7, 123.2, 122.6, 119.4, 116.2, 115.6, 114.8, 114.7, 111.8, 107.6, 105.4, 80.3, 80.1, 80.0, 60.7, 56.1, 55.6, 55.5, 54.3, 53.4, 52.1, 41.8, 38.1 (2C), 37.8, 28.2 (9C), 22.0. MS (ESI) m/z: 1295 $(M+23)^+$, 1273 $(M+1)^+$. Rf: 0.21 ($CH_2Cl_2$:MeOH, 50:1).

Example 126: Compound **126**



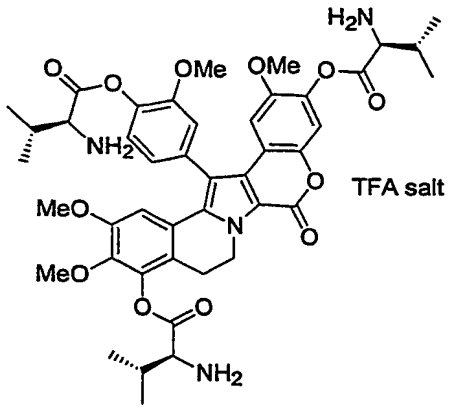
$Et_3N$ (23 ml, 0.1685 mmol) was added to a solution of **26** (16.0 mg, 0.0312 mmol) in $CH_2Cl_2$ (5 mL) a 0 °C under Argon atmosphere. $Tf_2NPh$ (33.4 mg, 0.0935 mmol) and DMAP (0.8 mg, 0.0069 mmol) were addded and the mixture was stirred at 23 °C for 2 h . Saturated aqueous solution of $NaHCO_3$ (5 mL) was added and the mixture was extracted with $CH_2Cl_2$, dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$) to give **126** as a pale yellow solid (24.2 mg, quant.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.16 (d, $J$= 7.3 Hz, 1H), 7.54 (d, $J$= 8.1 Hz, 1H), 7.40-7.25 (m, 2H), 7.20 (s, 1H), 7.11 (br s, 2H), 6.98 (s, 1H), 6.76 (s, 1H), 3.99 (s, 3H), 3.98 (s, 3H), 3.50 (s, 3H), 3.46 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.4, 152.6, 150.7, 149.8, 147.9, 144.9, 138.8, 137.7, 137.4, 134.3, 129.6, 127.5, 127.2, 125.0, 124.1, 123.7, 122.9, 118.6 (2C, t, $J_{C-F}$=172.7, 164.5 Hz), 116.3, 113.7, 112.0, 110.2, 107.7, 106.5, 104.7, 56.7, 56.0, 55.8, 55.2. MS (ESI) m/z: 778 $(M+1)^+$. Rf: 0.36 ($CH_2Cl_2$).

Example 127: Compound **127**



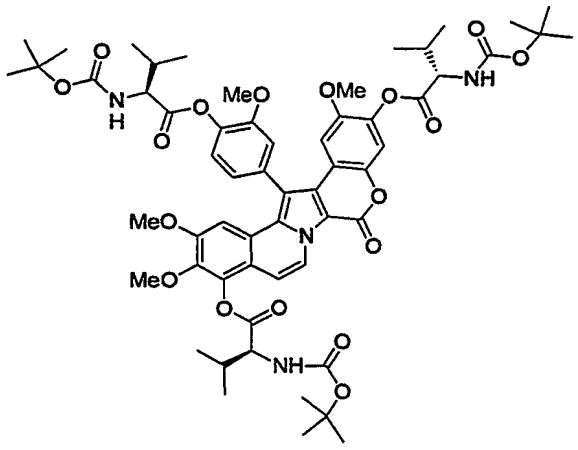

A suspension of **140** (45 mg, 0.041 mmol) and DDQ (19 mg, 0.082 mmol) in $CCl_4$ (2 mL) was refluxed for 17 h. The mixture was cooled at 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 30:1) to give **127** (30 mg, 67%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.27-9.23 (m, 1H), 7.47-7.36 (m, 1H), 7.26-7.08 (m, 6H), 6.84-6.78 (m, 1H), 4.56-4.49 (m, 3H), 3.80 (s, 3H), 3.66-3.47 (m, 6H), 3.43 (s, 6H), 2.40-2.29 (m, 6H), 2.04-1.98 (m, 6H), 1.49 (s, 27H). MS (ESI) m/z: 1091 $(M+1)^+$. Rf: 0.31 ($CH_2Cl_2$:MeOH 30:1).

Example 128: Compound **128**




TFA (1 mL) was added to a solution of **131** (26 mg, 0.023 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **128** was obtained as a white solid (25 mg, 99%). The solid was collected by triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.50-7.40 (m, 2H), 7.30-7.20 (m, 2H), 6.82 (d, $J$= 5.4 Hz, 1H), 6.79 (d, $J$= 7.9 Hz, 1H), 4.90-4.70 (m, 2H), 4.44 (d, $J$= 3.4 Hz, 1H), 4.32 (dd, $J$= 4.2 and 1.6 Hz, 1H), 4.24 (d, $J$= 4.3 Hz, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.44 (s, 3H), 3.43 (s, 3H), 3.15-3.00 (m, 2H), 2.65-2.40 (m, 3H), 1.30-1.15 (m, 18H). MS (ESI) m/z: 851 $(M+23)^+$, 829 $(M+1)^+$.

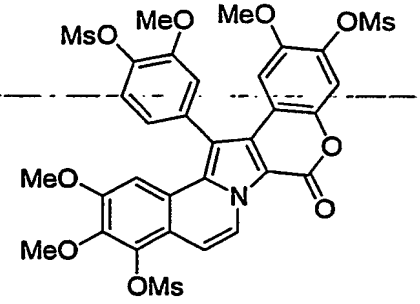
Example 129: Compound **129**




To a solution of **131** (67 mg, 0.059 mmol) in $CHCl_3$ (1 mL), DDQ (27 mg, 0.118 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 24 h. The reaction was followed by $^1H$ NMR. The reaction was cooled to 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 30:1) to give **129** as a yellow solid (53 mg, 79 %). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.21 (d, $J$= 7.6 Hz, 1H), 7.40-7.05 (m, 6H), 6.78 (d, $J$= 9.1 Hz, 1H), 5.15-5.05 (m, 3H), 4.65-4.50 (m, 3H), 3.86 (s, 3H), 3.81 (s, 3H), 3.48 (s, 3H), 3.42 (s, 3H), 2.50-2.30 (m, 3H), 1.49 (s, 18H), 1.46 (s, 9H), 1.25-0.95 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.2 (3C), 155.9, 155.7, 154.9, 153.1, 152.2, 147.6, 145.4, 145.3, 141.7, 139.9, 139.4, 138.7,

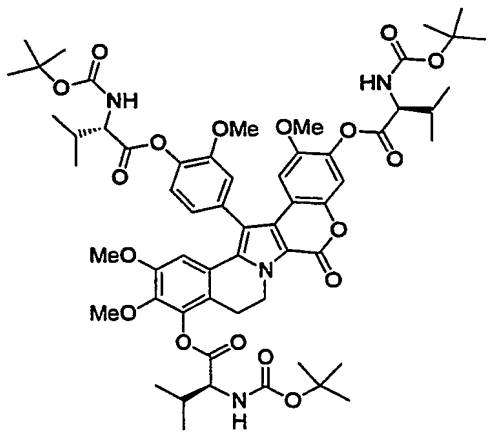
134.5, 133.1, 128.3 (2C), 124.0, 123.6, 123.5, 121.0, 118.3, 115.8, 115.1, 112.1, 109.0, 106.9, 106.1, 104.2, 80.3, 80.0 (2C), 60.7, 59.0, 58.6 (2C), 56.0, 55.7, 55.6, 31.3, 31.1, 30.9, 28.3 (9C), 19.3, 19.2, 19.0, 17.5, 17.2, 17.1. MS (ESI) m/z: 1149 $(M+23)^+$. Rf: 0.19 ($CH_2Cl_2$:MeOH, 50:1).

Example 130: Compound **130**




To a solution of **136** (26 mg, 0.034 mmol) in $CHCl_3$ (2 mL), DDQ (15 mg, 0.067 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 3 days. The reaction was followed by $^1H$ NMR and it was neccesary to add solvent to get a optimal mixture. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 30:1) to afford **130** as a brownish solid (105 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.15 (d, $J$= 7.6 Hz, 1H), 7.59 (d, $J$= 8.0 Hz, 1H), 7.37 (d, $J$= 7.5 Hz, 1H), 7.35-7.25 (m, 3H), 7.08 (s, 1H), 6.75 (s, 1H), 3.99 (s, 3H), 3.96 (s, 3H), 3.49 (s, 3H), 3.47 (s, 3H), 3.42 (s, 3H), 3.37 (s, 3H), 3.19 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 154.3, 153.1, 152.9, 148.0, 145.1, 142.6, 138.3, 138.2, 137.7, 135.7, 132.6, 127.6, 125.8, 123.8, 123.6, 121.0, 119.8, 116.6, 115.7, 113.7, 111.8, 109.1, 107.7, 106.4, 104.9, 61.5, 56.6, 55.8, 55.6, 39.7, 39.3, 38.6. MS (ESI) m/z: 764 $(M+1)^+$. Rf: 0.54 ($CH_2Cl_2$:MeOH, 50:1).

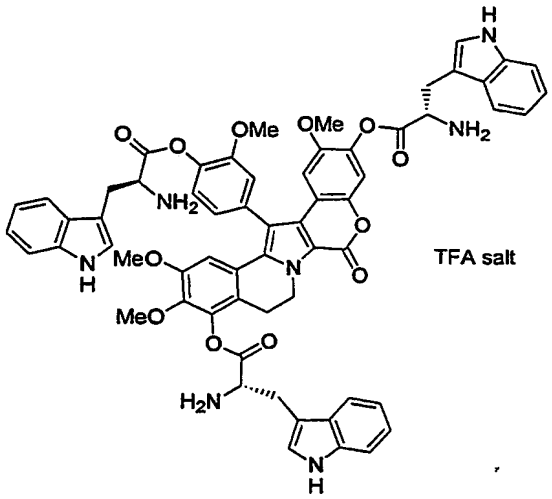
Example 131: Compound **131**




A suspension of **1** (50 mg, 0.094 mmol), (L)-N-Boc-Valine (122 mg, 0.56 mmol), EDC·HCl (108 mg, 0.56 mmol) and DMAP (7 mg, 0.056 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with $H_2O$ (2x20 mL) and saturated aqueous solution of

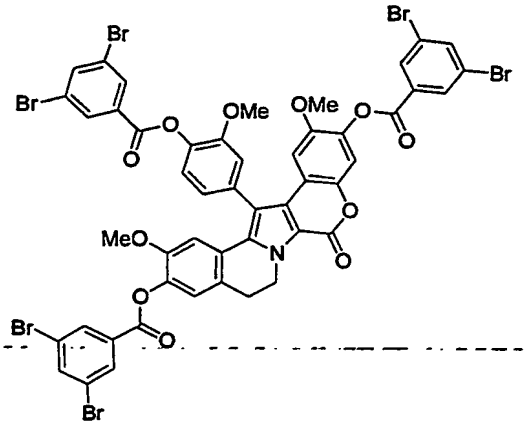
$NaHCO_3$ (2x20 mL), dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 50:1 to 30:1) to give **131** as a yellow solid (105 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.30-7.10 (m, 2H), 7.08 (s, 2H), 6.63 (t, $J$= 8.9 Hz, 2H), 5.10-5.10 (m, 3H), 4.70 (br s, 1H), 4.66 (br s, 1H), 4.60-4.45 (m, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.38 (s, 3H), 3.37 (s, 3H), 3.00 (br t, 2H), 2.45-2.30 (m, 3H), 1.48 (s, 9H), 1.47 (s, 9H), 1.45 (s, 9H), 1-15-0.95 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.6, 170.4 (2C), 155.7, 155.6, 154.9, 152.0, 151.8, 147.4, 144.8, 141.2, 141.0, 139.6, 138.5, 134.7, 134.3, 127.0, 126.9, 123.8, 123.2, 122.6, 119.4, 116.1, 115.6, 114.8, 114.7, 111.8, 107.6, 105.4, 80.1, 80.0, 79.9, 60.6, 58.8, 58.5, 58.4, 56.0, 55.6, 55.4, 41.8, 31.3, 31.1, 30.8, 28.3 (9C), 22.2, 19.2, 19.1, 19.0, 17.4, 17.1, 17.0. MS (ESI) m/z: 1151.7 $(M+23)^+$, 1129.8 $(M+1)^+$. Rf: 0.70 ($CH_2Cl_2$:MeOH, 20:1).

Example 132: Compound **132**



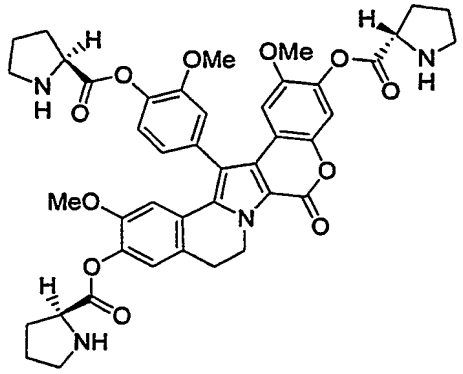

TFA (1 mL) was added to a solution of **137** (50 mg, 0.035 mmol) in anhydrous $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 1 h. The solvent was evaporated under reduced pressure and the mixture was treated with $CH_2Cl_2$ (3x5 mL) in order to remove the remaining TFA. After final evaporation to dryness **132** was obtained as a brownish solid (50 mg, quant.). The solid was collected by triturating in $Et_2O$ and filtrating. $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.90-7.40 (m, 19H), 6.80-6.70 (m, 2H), 4.90-4.50 (m, 5H), 3.90 (s, 3H), 3.79 (s, 3H), 3.60-3.30 (m, 12H), 2.72 (br s, 2H). MS (ESI) m/z: 1090 $(M)^+$.

Example 133: Compound **133**



A suspension of **109** (25 mg, 0.050 mmol), 3,5-dibromobenzoic acid (84 mg, 0.30 mmol), EDC·HCl (58 mg, 0.30 mmol) and DMAP (4 mg, 0.03 mmol) in anhydrous $CH_2Cl_2$ (5 mL) was stirred under Argon atmosphere at 23 °C for 6 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL), the aqueous phase was extracted with $CH_2Cl_2$ (10 mL), the organic phases were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 200:1 to 100:1) to give **133** as a white solid (43 mg, 67%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.28 (d, $J$= 1.8 Hz, 2H), 8.26 (d, $J$= 1.8 Hz, 2H), 8.24 (d, $J$= 1.8 Hz, 2H), 7.95-7.92 (m, 3H), 7.34 (d, $J$= 8.1 Hz, 1H), 7.26 (s, 1H), 7.24-7.20 (m, 2H), 7.08 (s, 1H), 6.88 (s, 1H), 6.81 (s, 1H), 4.94-4.89 (m, 1H), 4.81-4.77 (m, 1H), 3.83 (s, 3H), 3.49 (s, 3H), 3.43 (s, 3H), 3.17 (t, $J$= 6.7 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 169.9, 154.9, 151.9, 149.1, 147.6, 147.4, 144.7, 139.4, 138.3, 135.8, 134.4, 129.4, 129.2, 128.5, 127.1, 126.4, 126.3, 123.6, 123.3, 119.5, 116.3, 114.9, 114.6, 114.4, 111.7, 110.9, 108.4, 105.4, 79.9,79.9 (2C), 56.0, 55.8, 55.6, 55.4, 54.3 (2C), 42.4 38.0 (2C), 28.4, 28.2 (6C). MS (ESI) m/z: 1288 $(M+1)^+$. Rf: 0.72 ($CH_2Cl_2$).

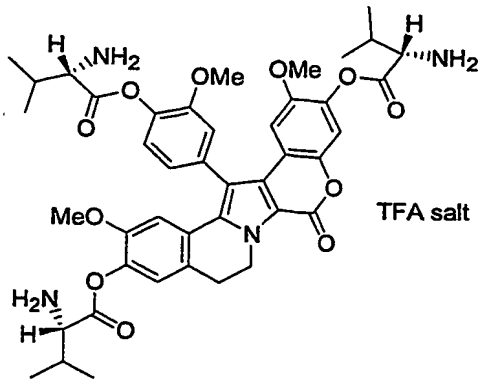
Example 134: Compound **134**



TFA (1 mL) was added to a solution of **140** (15 mg, 0.014 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 3 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **134** as a white solid (17 mg, quant.). $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.49-7.44 (m, 2H), 7.29-7.17 (m, 3H), 6.88-6.75 (m, 2H), 4.79-4.68 (m, 3H), 3.89 (s, 3H), 3.52-3.38 (m,

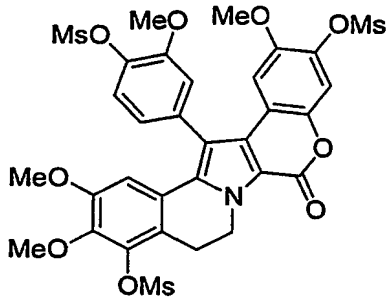
12H), 3.15 (br t, 2H), 2.63-2.35 (m, 6H), 2.25-2.15 (m, 6H). MS (ESI) m/z: 793 $(M+1)^+$.

Example 135: Compound **135**




TFA (1 mL) was added to a solution of **144** (15 mg, 0.0136 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 4 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **135** as a white solid (16 mg, quant.). $^1$H NMR (300 MHz, $CD_3OD$) $\delta$ 7.47-7.44 (m, 2H), 7.28 (d, $J$= 8.1 Hz, 1H), 7.19 (s, 1H), 7.15 (s, 1H), 6.90-6.78 (m, 2H), 4.77 (br t, 2H), 4.32 (s, 1H), 4.24 (s, 2H), 3.87 (s, 3H), 3.45 (s, 3H), 3.37 (s, 3H), 3.17 (br t, 2H), 2.54-2.46 (m, 3H), 1.26-1.17 (m, 18H). MS (ESI) m/z: 799 $(M+1)^+$.

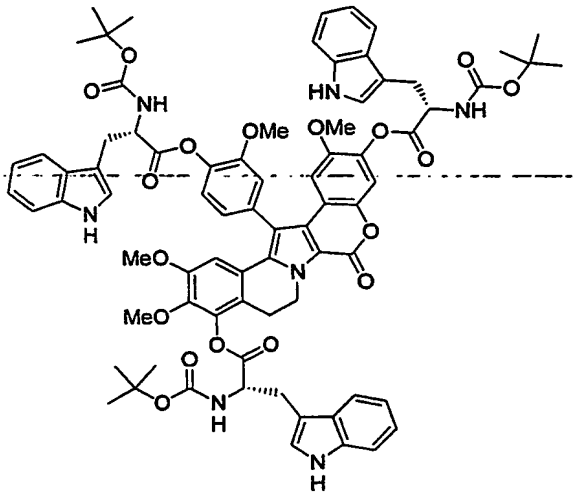
Example 136: Compound **136**



To a solution of **1** (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ (2 mL) under Argon at 0 °C, $Et_3N$ (39 µL, 0.28 mmol) and methanesulfonyl chloride (22 µL, 0.28 mmol) were added. The resulting mixture was stirred at 23 °C for 2 h, then quenched with $H_2O$ and extrated with $CH_2Cl_2$ (3x20 mL). The combined organic phases were washed with saturated aqueous solution of $NaHCO_3$, dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, 50:1) to afford **136** as a brownish solid (35 mg, 97%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.51 (d, $J$= 8.0 Hz, 1H), 7.30-7.15 (m, 3H), 6.66 (s, 1H), 6.63 (s, 1H), 5.00-4.90 (m, 1H), 4.75-4.50 (m, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.45 (s, 3H), 3.37 (s, 3H), 3.35 (s, 3H), 3.32 (s, 3H), 3.30-3.20 (m, 2H), 3.17 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 154.5, 152.8, 151.9, 148.0, 144.7, 141.8, 141.0, 138.0, 137.0, 135.6, 134.4, 126.3, 125.6, 123.5, 123.1,

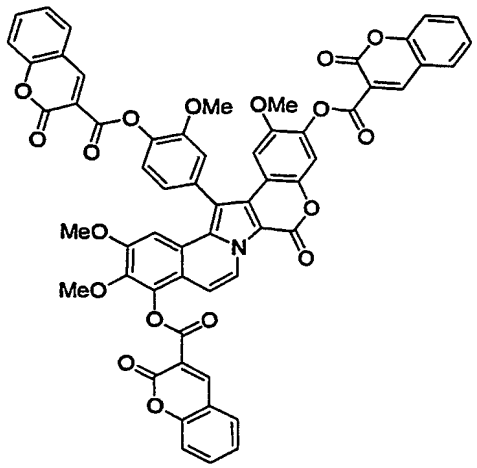
121.7, 117.0, 115.5, 115.3, 113.6, 108.2, 105.7, 61.3, 56.5, 55.8, 55.5, 42.0, 39.4, 39.2, 38.6, 23.3. MS (ESI) m/z: 766 $(M+1)^+$. Rf: 0.54 ($CH_2Cl_2$:MeOH, 50:1).

Example 137: Compound **137**



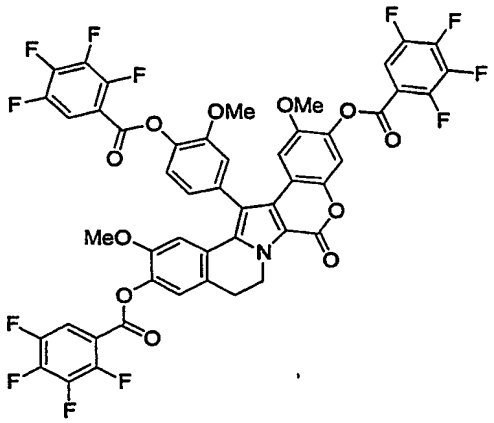
A suspension of **1** (50 mg, 0.094 mmol), (L)-N-Boc-Trp (172 mg, 0.56 mmol), EDC·HCl (108 mg, 0.56 mmol) and DMAP (7 mg, 0.056 mmol) in $CH_2Cl_2$ (4 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was diluted with $CH_2Cl_2$ (50 mL), washed with $H_2O$ (2x20 mL) and saturated aqueous solution of $NaHCO_3$ (2x20 mL), dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 30:1 to 20:1) to give **137** as a brown solid (130 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.51 (s, 2H), 8.42 (br s, 1H), 7.70-7.60 (m, 3H), 7.45-7.30 (m, 3H), 7.30-6.95 (m, 9H), 6.87 (s, 1H), 6.70-6.55 (m, 2H), 5.30-5.15 (m, 2H), 5.10-4.90 (m, 3H), 4.80-4.40 (m, 2H), 3.76 (s, 6H), 3.60-3.30 (m, 12H), 2.70 (br s, 2H), 1.45 (s, 27H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.8, 170.4 (2C), 155.2, 154.9, 152.0, 151.7, 147.5, 144.6, 141.4, 141.0, 139.6, 138.5, 136.1 (2C), 134.7, 134.1, 127.7, 127.6, 126.8, 123.8, 123.4, 123.1 (2C), 122.6, 122.2, 119.7, 119.6 (2C), 118.7, 118.6, 116.0, 115.6, 114.6, 111.7, 111.3 (2C), 109.8, 109.4, 107.6, 105.4, 80.2, 80.0 (2C), 60.8, 56.1, 55.6, 55.5, 54.4 (2C), 53.4, 41.7, 28.2 (9C+3C), 21.7. MS (ESI) m/z: 1412 $(M+23)^+$, 1391 $(M+1)^+$. Rf: 0.22 ($CH_2Cl_2$:MeOH, 30:1).

Example 138: Compound **138**



To a solution of **149** (35 mg, 0.033 mmol) in $CCl_4$ (2 mL) DDQ (15 mg, 0.066 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 80 °C for 2 days. The reaction was followed by $^1H$ NMR and it was neccesary to add solvent to get an optimal mixture. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, from 100:1 to 50:1) to afford **138** as a white solid (29 mg, 83%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.17 (d, $J$= 7.6 Hz, 1H), 8.85 (d, $J$= 4.5 Hz, 2H), 8.78 (s, 1H), 7.80-7.60 (m, 6H), 7.55-7.20 (m, 11H), 7.18 (s, 1H), 6.89 (s, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.60 (s, 3H), 3.53 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 161.2, 160.6, 160.3, 156.4, 156.2, 155.5, 155.4, 155.3, 154.8, 153.3, 152.4, 150.5, 150.4, 150.1, 147.7, 145.4, 141.8, 139.9, 139.4, 138.7, 135.1, 135.0, 134.9, 134.7, 133.2, 129.9, 129.8, 129.7, 128.2, 125.1, 125.0, 124.9, 124.1, 123.7, 123.4, 120.9, 118.2, 117.8, 117.7, 117.7, 116.9, 116.7, 116.5, 115.9, 115.4, 112.3, 112.1, 109.0, 106.9, 106.3, 104.4, 61.0, 56.4, 56.1, 55.9. MS (ESI) m/z: 1046 $(M+1)^+$. Rf: 0.50 ($CH_2Cl_2$:MeOH, 50:1).

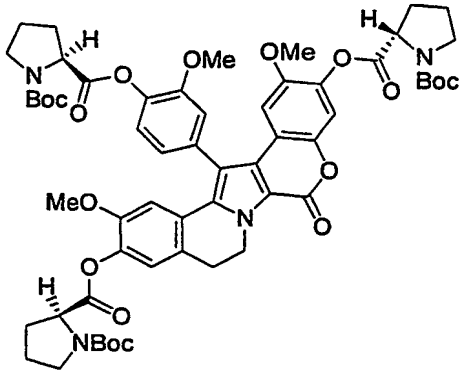
Example 139: Compound **139**



A suspension of **109** (25 mg, 0.050 mmol), 2,3,4,5-tetrafluorobenzoic acid (58 mg, 0.30 mmol), EDC·HCl (58 mg, 0.30 mmol) and DMAP (4 mg, 0.03 mmol) in anhydrous $CH_2Cl_2$ (5 mL) was stirred under Argon atmosphere at 23 °C for 6 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL), the aqueous phase was extracted with $CH_2Cl_2$ (10mL), the combined organic phases were dried over anhydrous $Na_2SO_4$ and

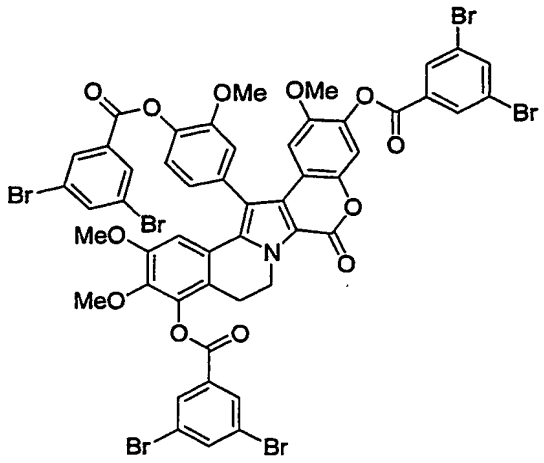
the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 200:1) to give **139** as a white solid (33 mg, 64%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.81-7.74 (m, 3H), 7.36 (d, $J$= 8.1 Hz, 1H), 7.25 (s, 1H), 7.23 (s, 1H), 7.19 (s, 1H), 7.10 (s, 1H), 6.86 (s, 1H), 6.78 (s, 1H), 4.97-4.91 (m, 1H), 4.82-4.77 (m, 1H), 3.83 (s, 3H), 3.48 (s, 3H), 3.41 (s, 3H), 3.17 (t, $J$= 6.5 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 159.6 (3C), 154.9, 152.1, 149.7, 147.5, 144.9, 139.5, 138.9, 138.3, 134.9, 134.7, 126.9, 126.2, 126.1, 123.7, 123.3, 122.5, 116.5, 115.9, 115.2, 114.9, 113.8, 113.5, 111.9, 109.9, 105.6, 56.3, 55.9, 55.7, 42.5, 28.1. MS (ESI) m/z: 1030 $(M+1)^+$. Rf: 0.50 ($CH_2Cl_2$:MeOH, 200:1).

Example 140: Compound **140**



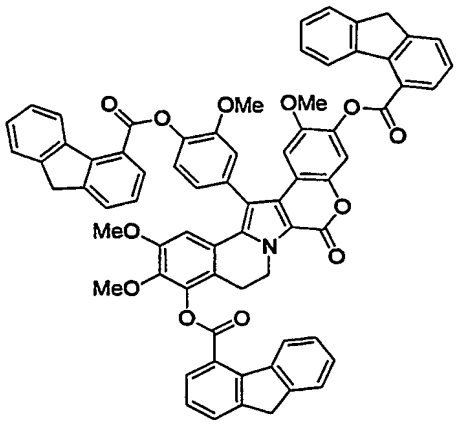

A suspension of **109** (50 mg, 0.0997 mmol), Boc-L-Pro-OH (86 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in anhydrous $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 4 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL). The aqueous phase was extracted with $CH_2Cl_2$ (10mL). The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 100:1 to 50:1) to give **140** as a white solid (74 mg, 68%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.16-7.13 (m, 2H), 7.06-7.03 (m, 2H), 6.90 (s, 1H), 6.78-6.63 (m, 2H), 4.95-4.62 (m, 2H), 4.56-4.46 (m, 3H), 3.78 (s, 3H), 3.69-3.43 (m, 6H), 3.40 (s, 3H), 3.33 (s, 3H), 3.11 (br t, 2H), 2.40-2.26 (m, 6H), 2.08-1.90 (m, 6H), 1.47 (s, 27H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.0, 170.8, 170.7, 155.0, 154.3, 153.7, 153.7 (2C), 152.1, 149.7, 147.6, 144.8, 139.8, 139.3, 138.7, 134.1, 125.9, 125.6, 124.0, 123.4, 123.1 (2C), 122.7, 122.2, 116.0, 114.7, 111.6, 109.6, 105.3, 80.1, 80.0, 79.8, 58.9 (2C), 56.1, 55.7, 55.6, 55.5, 46.5, 46.3 (2C), 42.4, 31.5, 30.9, 29.9, 28.3 (9C), 28.0, 24.2, 23.4, 22.5. MS (ESI) m/z: 1115 $(M+23)^+$, 1093 $(M+1)^+$. Rf: 0.18 ($CH_2Cl_2$:MeOH, 50:1).

Example 141: Compound **141**



To a solution of **1** (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ (2 mL) under Argon at 23 °C, 3,5-dibromo-benzoic acid (79 mg, 0.28 mmol), EDC·HCl (54 mg, 0.28 mmol) and DMAP (4 mg, 0.028 mmol) were added and the mixture stirred for 4 h. $CH_2Cl_2$ (50 mL) was added and then washed with $H_2O$ (2x10 mL) and saturated aqueous solution of $NaHCO_3$ (2x10 mL), dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, 200:1) to afford **141** as a white solid (61 mg, 98%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.32 (d, $J$= 1.7 Hz, 2H), 8.30 (d, $J$= 1.8 Hz, 2H), 8.26 (d, $J$= 1.7 Hz, 2H), 7.98 (t, $J$= 1.7 Hz, 1H), 7.96 (t, $J$= 1.7 Hz, 1H), 7.93 (t, $J$= 1.8 Hz, 1H), 7.36 (d, $J$= 7.8 Hz, 1H), 7.25-7.19 (m, 3H), 6.78 (s, 1H), 6.77 (s, 1H), 5.00-4.60 (br s, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 3.48 (s, 6H), 3.10-3.00 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 162.3, 152.5, 152.2, 147.9, 145.2, 141.6, 140.0, 139.5, 139.2, 138.9, 135.1, 134.8, 132.5, 132.2, 129.1, 127.3, 124.0, 123.7, 123.6, 123.5, 123.4, 123.0, 119.3, 116.7, 116.0, 115.1, 112.2, 108.1, 105.8, 61.2, 56.5, 56.1, 55.9, 42.2, 22.6. MS (ESI) m/z: 1319 $(M+1)^+$. Rf: 0.58 ($CH_2Cl_2$).

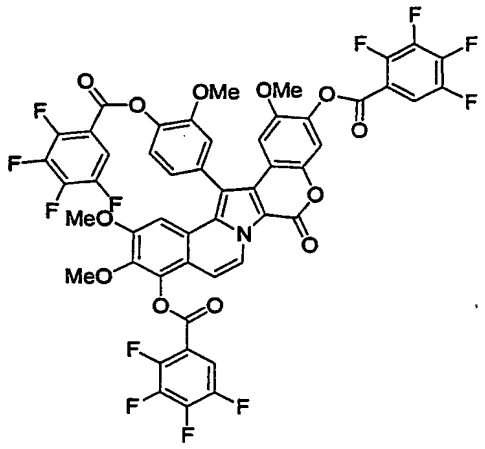
Example 142: Compound **142**



To a solution of **1** (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ (2 mL) under Argon at 23 °C, 4-fluorenecarboxylic acid (59 mg, 0.28 mmol), DCC (58 mg, 0.28 mmol) and DMAP (4 mg, 0.028 mmol) were added and the mixture stirred for 4 h $CH_2Cl_2$ (50 mL) was added and then washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL), dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, from 200:1 to 100:1) to

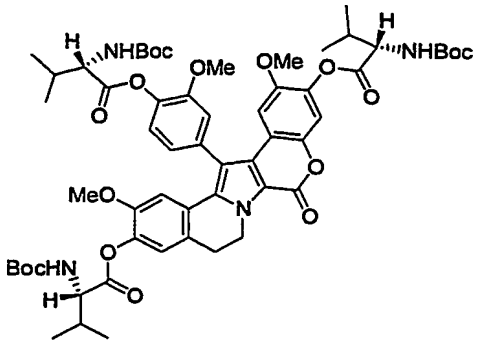
afford **142** as a white solid (36 mg, 69%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.60-8.40 (m, 3H), 8.30-8.10 (m, 3H), 7.90-7.70 (m, 3H), 7.65-7.55 (m, 3H), 7.55-7.25 (m, 13H), 6.92 (s, 1H), 6.91 (s, 1H), 5.10-4.70 (br s, 2H), 4.00 (s, 2H), 3.99 (s, 2H), 3.96 (s, 2H), 3.93 (s, 3H), 3.91 (s, 3H), 3.60 (s, 3H), 3.58 (s, 3H), 3.18 (br s, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.0, 165.9, 155.1, 152.6, 152.1, 148.0, 145.4. 145.2, 145.1, 145.0, 144.3, 144.2, 144.1, 141.9, 141.8, 141.5, 141.3, 140.4, 140.0, 139.9, 139.8, 139.2, 135.0, 134.3, 129.5, 129.4, 129.3, 129.0, 127.8, 127.7, 127.6, 127.3, 127.0, 126.8, 126.7, 126.2, 126.1, 126.0, 125.4, 125.3, 125.1, 125.0, 124.7, 124.5, 124.1, 123.5, 122.9, 119.6, 116.2, 116.0, 114.9, 112.1, 107.7, 105.6, 61.0, 56.3, 55.8, 55.7, 42.0, 37.0 (3C), 22.5. MS (ESI) m/z: 1108 $(M)^+$. Rf: 0.34 ($CH_2Cl_2$).

Example 143: Compound **143**



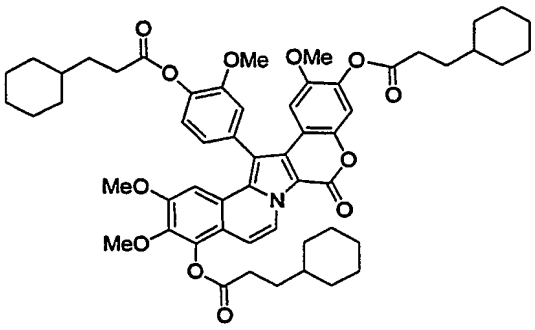

To a solution of **99** (30 mg, 0.028 mmol) in $CHCl_3$ (1 mL), DDQ (13 mg, 0.056 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 63 h. The reaction was followed by $^1$H NMR. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, 200:1) to afford **143** as a white solid (27 mg, 93%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.5 Hz, 1H), 7.95-7.70 (m, 3H), 7.46 (d, $J$= 8.2 Hz, 1H), 7.40-7.35 (m, 2H), 7.25 (s, 1H), 7.18 (s, 1H), 7.11 (d, $J$= 7.6 Hz, 1H), 6.88 (s, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.58 (s, 3H), 3.51 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 154.7, 153.3, 152.3, 147.6, 145.4, 143.1, 141.7, 139.7, 139.2, 138.5, 135.0, 133.1, 128.2, 123.9, 123.7, 123.6, 120.9, 117.9, 116.1, 115.3, 113.8, 112.1, 109.1, 106.4, 106.3, 104.6, 61.0, 56.4, 55.9, 55.7. MS (ESI) m/z: 1058 $(M+1)^+$. Rf: 0.54 ($CH_2Cl_2$).

Example 144: Compound **144**



A suspension of **109** (50 mg, 0.0997 mmol), Boc-L-Val-OH (87 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in anhydrous $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 4 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and saturated aqueous solution of $NaHCO_3$ (10 mL). The aqueous phase was extracted with $CH_2Cl_2$ (10 mL). The combined organic phases were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 100:1 to 50:1) to give **144** as a white solid (87 mg, 79%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.26-7.13 (m, 2H), 7.09 (s, 2H), 6.96 (s, 1H), 6.76 (d, $J$= 7.5 Hz, 1H), 6.68 (d, $J$= 9.5 Hz, 1H), 5.08-5.05 (m, 3H), 4.91-4.69 (m, 2H), 4.52-4.46 (m, 3H), 3.77 (s, 3H), 3.40 (s, 3H), 3.32 (s, 3H), 3.18 (br t, 2H), 2.42-2.38 (m, 3H), 1.48 (s, 9H), 1.45 (s, 18H), 1.11-0.98 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 170.3 (3C), 155.6, 154.9, 152.1, 149.7, 147.5, 144.8, 139.7, 139.1, 138.5, 134.9, 134.2, 126.9, 126.0, 125.7, 123.8, 123.1, 122.5, 116.1, 115.8, 115.0, 114.6, 111.9, 109.6, 105.4, 79.9 (3C), 58.5, 56.0, 55.6, 55.3, 55.3, 53.4, 42.4, 31.2 (3C), 28.3 (9C), 28.0, 19.1 (2C), 17.1 (4C). MS (ESI) m/z: 1121 $(M+23)^+$, 1099 $(M+1)^+$. Rf: 0.35 ($CH_2Cl_2$:MeOH, 50:1).

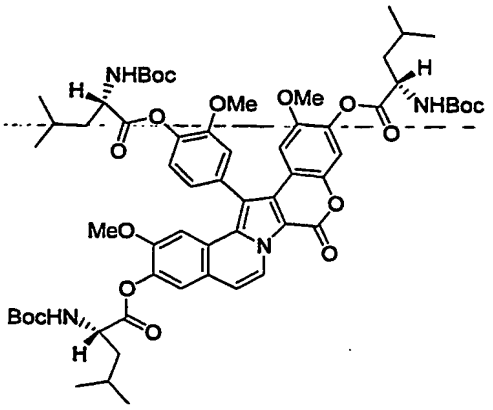
Example 145: Compound **145**



To a solution of **148** (31 mg, 0.032 mmol) in $CHCl_3$ (2 mL), DDQ (11 mg, 0.049 mmol) was added. The resulting mixture was heated in a sealed bottom flask at 65 °C for 24 h. The reaction was followed by $^1H$ NMR. The reaction was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$. The organic solvent was removed under vacuum and the resulting residue purified on silica gel ($CH_2Cl_2$:MeOH, 200:1) to afford **145** as a white solid (27 mg, 87%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.5 Hz, 1H), 7.35-7.00 (m, 6H), 6.81 (s, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.49 (s, 3H), 3.45 (s, 3H), 2.76 (t, $J$= 7.6 Hz, 2H), 2.70-2.55 (m, 4H), 1.90-1.60 (m, 18H), 1.50-1.10 (m, 15H), 1.05-0.80 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 172.0, 171.9, 171.8, 155.0, 153.2, 152.4, 147.8, 145.5, 141.8, 140.4, 139.9, 139.1, 134.1, 133.3, 128.4, 124.1,

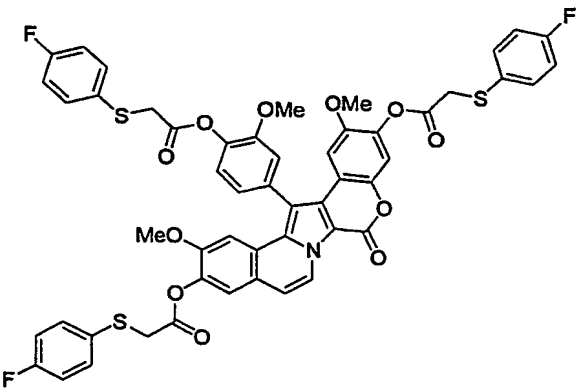
123.6, 123.3, 121.0, 118.3, 116.5, 115.5, 115.0, 112.2, 108.9, 106.6, 106.1, 104.0, 60.8, 56.2, 55.7, 55.6, 37.2, 37.1, 37.0, 33.0 (4C), 32.9 (4C), 32.4, 32.3, 32.2, 31.6, 31.5, 26.5, 26.2 (6C). MS (ESI) m/z: 944 $(M)^+$. Rf: 0.35 ($CH_2Cl_2$).

Example 146: Compound **146**




A suspension of **153** (52 mg, 0.046 mmol) and DDQ (16 mg, 0.068 mmol) in $CHCl_3$ (5 mL) was refluxed for 35 h. The mixture was cooled at 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 100:1) to give **146** (38 mg, 73%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.3 Hz, 1H), 7.42 (s, 1H), 7.32 (d, $J$= 7.9 Hz, 1H), 7.25-7.17 (m, 4H), 7.05 (d, $J$= 7.7 Hz, 1H), 6.79 (d, $J$= 5.9 Hz, 1H), 4.98-4.96 (m, 3H), 4.62-4.56 (m, 3H), 3.80 (s, 3H), 3.44 (s, 3H), 3.43 (s, 3H), 1.87-1.64 (m, 9H), 1.49 (s, 9H), 1.46 (s, 18H), 1.06-0.99 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.4 (4C), 155.3, 155.0, 152.3, 150.9, 147.7, 145.4, 140.7, 140.1, 139.6, 134.4, 128.1, 124.0, 123.8, 123.6, 123.2, 120.7, 115.8, 115.1, 112.8, 112.3, 112.2, 109.1, 106.4, 106.2, 80.0 (3C), 56.2 (2C), 55.8 (2C), 55.7, 52.2, 41.7 (2C), 41.5, 28.3 (9C), 24.8 (3C), 23.0, 22.9 (3C), 21.9. MS (ESI) m/z: 1161 $(M+23)^+$, 1139 $(M+1)^+$. Rf: 0.45 ($CH_2Cl_2$:MeOH, 50:1).

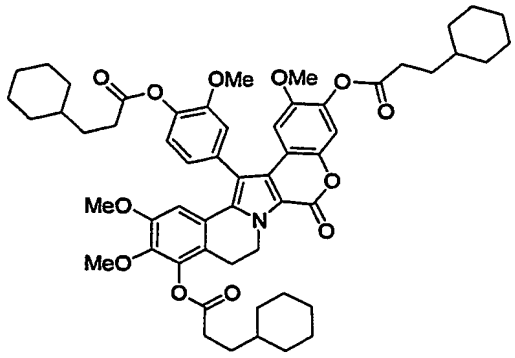
Example 147: Compound **147**




A suspension of **152** (26 mg, 0.026 mmol) and DDQ (9 mg, 0.039 mmol) in $CHCl_3$ (1.5 mL) was refluxed for 40 h. The mixture was cooled at 23 °C, filtered through Celite, and washed with $CH_2Cl_2$ (50 mL). The filtrated was concentrated under reduced

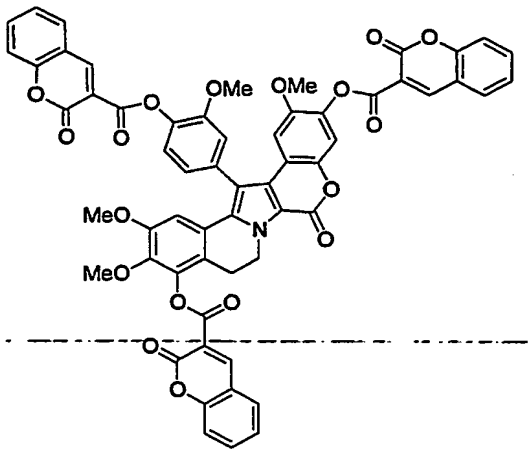
pressure and the residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, from 200:1 to 100:1) to give **147** (17 mg, 65%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.21 (d, $J$= 7.3 Hz, 1H), 7.58-7.50 (m, 6H), 7.31 (s, 1H), 7.21-7.16 (m, 4H), 7.10-7.01 (m, 8H), 6.75 (s, 1H), 3.87 (s, 2H), 3.84 (s, 2H), 3.81 (s, 2H), 3.78 (s, 3H), 3.37 (s, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 167.6, 167.5 (2C), 162.6 (d, $J_{C-F}$= 248.3, 3C), 154.9, 152.3, 150.8, 147.6, 145.4, 140.6, 140.0, 139.5, 134.6, 133.9, 133.8, 133.8, 133.7, 133.6, 133.4, 129.5, 129.3, 128.1, 123.8, 123.6, 123.2, 120.5, 116.4 (6C), 116.1 (6C), 115.9, 115.1, 112.8, 112.3, 112.0, 109.1, 106.4, 106.2. MS (ESI) m/z: 1026 $(M+23)^+$, 1004 $(M+1)^+$. Rf: 0.35 ($CH_2Cl_2$).

Example 148: Compound **148**



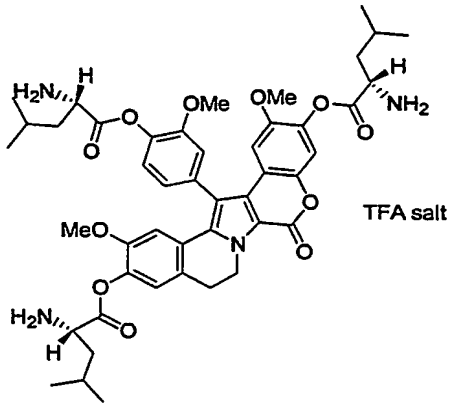

To a solution of **1** (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ (2 mL) under Argon at 23 °C, 3-cyclohexyl-propionic acid (44 mg, 0.28 mmol), EDC·HCl (54 mg, 0.28 mmol) and DMAP (4 mg, 0.028 mmol) were added and the mixture stirred for 3 h. $CH_2Cl_2$ (50 mL) was added and then washed with $H_2O$ (2x10 mL) and saturated aqueous solution of $NaHCO_3$ (2x10 mL), dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, 100:1) to afford **148** as a white solid (43 mg, 95%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.30-7.05 (m, 4H), 6.68 (s, 2H), 5.00-4.80 (m, 1H), 4.80-4.70 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.42 (s, 3H), 3.39 (s, 3H), 3.00-2.90 (m, 2H), 2.70-2.50 (m, 6H), 1.90-1.60 (m, 21H), 1.50-1.10 (m, 12H), 1.05-0.90 (m, 6H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.9, 171.9, 171.8, 155.1, 152.3, 151.8, 147.7, 144.9, 141.6, 141.2, 140.1, 139.1, 134.9, 133.9, 127.2, 123.9, 123.2, 122.6, 119.2, 115.9, 115.8, 114.7, 114.6, 111.9, 107.4, 105.4, 60.7, 56.2, 55.7, 55.5, 41.9, 37.2, 37.1, 37.0, 33.0 (4C), 32.9 (4C), 32.4, 32.3, 32.2, 31.6, 31.5, 31.4, 26.5, 26.3 (2C), 26.2 (2C), 26.1(2C), 22.2. MS (ESI) m/z: 946 $(M)^+$. Rf: 0.37 ($CH_2Cl_2$:MeOH, 100:1).

Example 149: Compound **149**



To a solution of **1** (25 mg, 0.047 mmol) in anhydrous $CH_2Cl_2$ (2 mL) under Argon at 23 °C, coumarin-3-carboxylic acid (54 mg, 0.28 mmol), EDC·HCl (54 mg, 0.28 mmol) and DMAP (4 mg, 0.028 mmol) were added and the mixture stirred for 3 h. $CH_2Cl_2$ (50 mL) was added and then washed with $H_2O$ (2x10 mL) and saturated aqueous solution of $NaHCO_3$ (2x10 mL), dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. The resulting residue was purified on silica gel ($CH_2Cl_2$:MeOH, 50:1) to afford **149** as a white solid (49 mg, 99%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.82 (s, 1H), 8.80 (s, 1H), 8.77 (s, 1H), 7.80-7.60 (m, 6H), 7.25-7.15 (m, 7H), 7.15-7.05 (m, 3H), 6.78 (s, 1H), 6.76 (s, 1H), 5.00-4.80 (br s, 1H), 4.80-4.60 (br s, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.50 (s, 3H), 3.48 (s, 3H), 3.20-3.05 (br s, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 161.2, 160.5, 160.4, 156.4, 156.3, 156.2, 155.5, 155.4, 154.9, 152.2, 151.9, 150.5, 150.4, 150.0, 149.1, 147.7, 144.9, 141.4, 141.1, 139.7, 138.6, 135.1, 135.0, 134.9, 134.8, 134.5, 129.9, 129.8, 129.7, 129.5, 127.0, 125.1, 125.0, 124.9, 123.9, 123.3, 122.7, 119.3, 117.8, 116.9, 116.8, 116.6, 116.3, 115.7, 114.9, 112.0, 107.9, 105.6, 61.0, 56.4, 56.0, 55.8, 41.9, 22.3. MS (ESI) m/z: 1048 $(M+1)^+$. Rf: 0.50 ($CH_2Cl_2$:MeOH, 50:1).

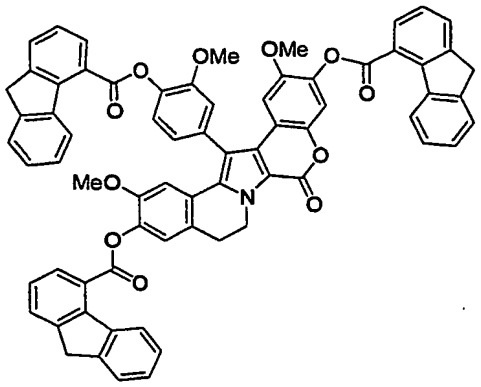
Example 150: Compound **150**



TFA (1 mL) was added to a solution of **153** (15 mg, 0.013 mmol) in $CH_2Cl_2$ (3 mL) at 0 °C under Argon atmosphere. The reaction mixture was stirred at 23 °C for 5 h. The solvent was evaporated under reduced pressure and in order to eliminate the remaining TFA, the mixture was treated with $CH_2Cl_2$ (3x15 mL) and evaporated to dryness to give **150** as a white solid (14 mg, 88%). $^1H$ NMR (300 MHz, $CD_3OD$) $\delta$ 7.47-7.41 (m, 2H),

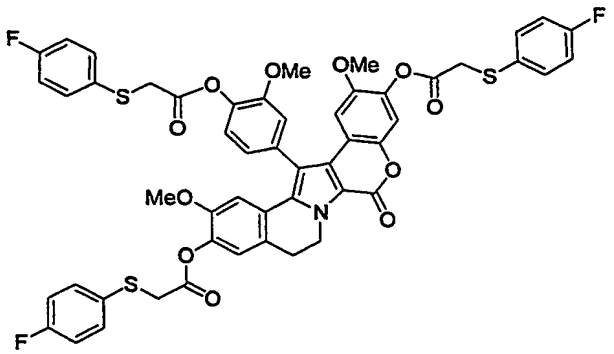
7.29-7.24 (m, 2H), 7.16 (s, 1H), 6.87 (d, $J$= 8.2 Hz, 1H), 6.80 (d, $J$= 10.1 Hz, 1H), 4.42-4.29 (m, 3H), 3.92-3.87 (m, 2H), 3.85 (s, 3H), 3.45 (s, 3H), 3.37 (s, 3H), 3.18 (t, $J$= 6.2 Hz, 2H), 2.14-1.61 (m, 9H), 1.12-0.98 (m, 18H). MS (ESI) m/z: 841 $(M+1)^+$.

Example 151: Compound **151**




A suspension of **109** (25 mg, 0.050 mmol), 9H-fluorene-4-carboxylic acid (63 mg, 0.30 mmol), EDC·HCl (58 mg, 0.30 mmol) and DMAP (4 mg, 0.03 mmol) in anhydrous $CH_2Cl_2$ (5 mL) was stirred under Argon atmosphere at 23 °C for 2 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL), the aqueous phase was extracted with $CH_2Cl_2$ (10 mL), the combined organic phases were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 200:1) to give **151** as a white solid (26 mg, 48%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.56-8.52 (m, 2H), 8.46-8.43 (m, 1H), 8.18-8.11 (m, 3H), 7.77-7.74 (m, 3H), 7.58-7.56 (m, 3H), 7.50-7.30 (m, 13H), 7.21 (s, 1H), 7.04 (s, 1H), 6.93 (s, 1H), 5.04-4.95 (m, 1H), 4.92-4.83 (m, 1H), 3.96 (s, 6H), 3.93 (s, 3H), 3.62 (s, 3H), 3.54 (s, 3H), 3.25 (t, $J$= 6.5 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 166.1, 166.0, 166.0, 155.2, 152.6, 150.2, 148.0, 145.2, 145.2, 145.1, 144.2, 144.2, 144.2, 141.5, 141.3, 140.4, 139.9, 139.8, 139.2, 135.2, 134.3, 129.5, 129.3, 129.1, 129.0, 127.7, 127.3, 126.9, 126.8, 126.1, 126.1, 126.0, 125.9, 125.4, 125.1, 125.1, 125.0, 124.7, 124.6, 124.1, 123.4, 122.8, 116.3, 116.1, 115.1, 114.8, 112.2, 109.9, 105.7, 56.3, 55.9, 55.7, 42.6, 37.0 (3C), 28.2. MS (ESI) m/z: 1100 $(M+23)^+$. Rf: 0.47 ($CH_2Cl_2$).

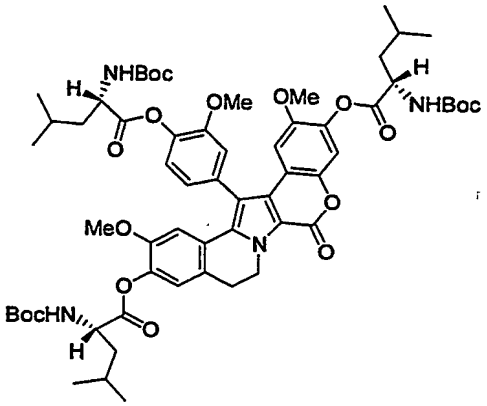
Example 152: Compound **152**




A suspension of **109** (25 mg, 0.050 mmol), fluorphenylsulfanylacetic acid (56 mg, 0.30 mmol), EDC·HCl (58 mg, 0.30 mmol) and DMAP (4 mg, 0.03 mmol) in anhydrous

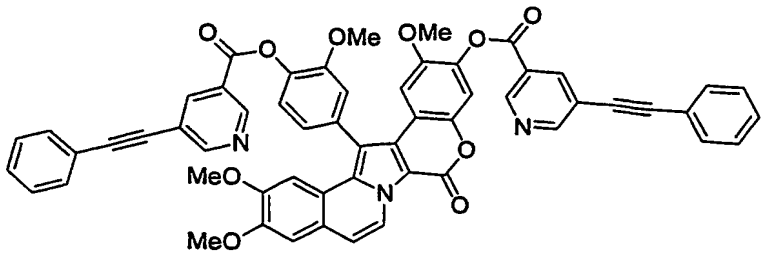
$CH_2Cl_2$ (5 mL) was stirred under Argon atmosphere at 23 °C for 2 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL), the aqueous phase was extracted with $CH_2Cl_2$ (10 mL) and combined the organic phases were dried over anhydrous $Na_2SO_4$ and the solvent removed under vacuum. The residue was purified by chromatography on silica gel (hexane:EtOAc, 60:40) to give **152** as a white solid (47 mg, 94%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.57-7.49 (m, 6H), 7.16-7.00 (m, 10H), 6.86 (s, 1H), 6.74 (s, 1H), 6.64 (s, 1H), 4.89-4.85 (m, 1H), 4.75-4.70 (m, 1H), 3.85 (s, 2H), 3.79 (s, 4H), 3.75 (s, 3H), 3.34 (s, 3H), 3.28 (s, 3H), 3.09 (t, $J$= 6.6 Hz, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 167.7, 167.5, 167.4, 164.2, 160.9, 154.9, 152.1, 149.7, 147.5, 144.8, 139.7, 139.2, 138.6, 134.9, 134.3, 133.8, 133.7, 133.6, 133.6, 129.3, 129.3, 126.9, 125.9, 125.8, 123.6, 123.1, 122.3, 116.4 (6C), 116.2, 116.1 (6C), 115.8, 115.0, 114.7, 111.7, 109.7, 105.5, 56.1, 55.6, 55.4, 42.4, 37.5 (3C), 27.8. MS (ESI) m/z: 1006 $(M+1)^+$. Rf: 0.40 (hexane:EtOAc, 60:40).

Example 153: Compound **153**



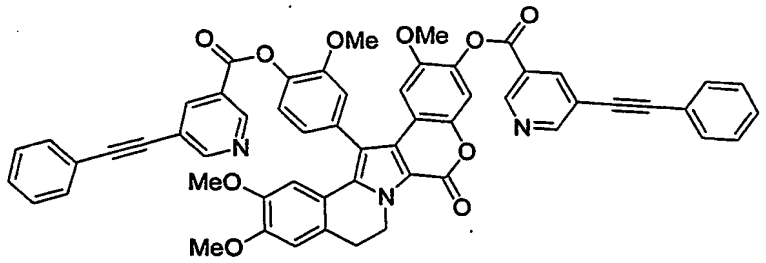

A suspension of **109** (50 mg, 0.0997 mmol), Boc-L-Leu-OH·$H_2O$ (99 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in anhydrous $CH_2Cl_2$ (4.3 mL) was stirred under Argon atmosphere at 23 °C for 3 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and HCl 0.1 N (10 mL) and the aqueous phases were extracted with $CH_2Cl_2$ (10 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give **153** as a white solid (77 mg, 68%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.24-7.08 (m, 4H);,6.99 (s, 1H), 6.76 (d, $J$= 7.0 Hz, 1H), 6.69 (d, $J$= 8.4 Hz, 1H), 4.94-4.86 (m, 3H), 4.78-4.68 (m, 1H), 4.63-4.50 (m, 2H), 4.37-4.26 (m, 2H), 3.78 (s, 3H), 3.41 (s, 3H), 3.34 (s, 3H), 3.12 (br t, 2H), 1.90-1.60 (m, 9H), 1.45 (s, 27H), 1.05-0.95 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 177.6 (2C), 171.4, 155.6, 155.4, 155.1, 152.1, 149.7, 147.6, 144.8, 139.8, 139.2, 138.7, 135.0, 134.1, 127.0, 127.0, 126.0, 125.7, 123.8, 123.1, 122.5, 116.1, 115.8, 114.9, 114.7, 111.9, 109.7, 105.5, 80.0 (3C), 56.1, 55.7, 55.5, 53.1, 52.2 (2C), 42.4, 41.5 (3C), 28.3 (9C), 28.0, 24.7 (2C), 22.9, 22.8 (4C), 21.8 (2C). MS (ESI) m/z: 1163 $(M+23)^+$, 1141 $(M+1)^+$. Rf: 0.26 (hexane:EtOAc, 2:1).

Example 154: Compound **154**



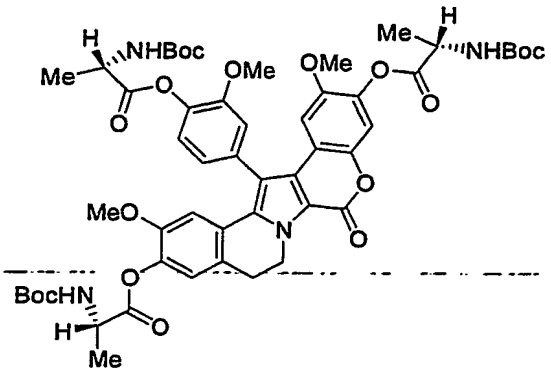
A suspension of **26** (19.5 mg, 0.038 mmol), 5-(2-phenyleth-1-ynyl)nicotinic acid (33.9 mg, 0.152 mmol), EDC·HCl (29.1 mg, 0.152 mmol) and DMAP (7.0 mg, 0.0573 mmol) in $CH_2Cl_2$ (5 mL) was stirred at 23 °C for 2 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:EtOAc, 4:1) to give **154**as a pale yellow solid (31.0 mg, 88%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$9.34-9.28 (m, 3H), 9.00-8.97 (m, 2H), 8.63-8.57 (m, 2H), 7.60-7.55 (m, 5H), 7.47-7.31 (m, 9H), 7.28 (s, 1H), 7.15-7.12 (m, 2H), 6.96 (s, 1H), 4.02 (s, 3H), 3.85 (s, 3H), 3.60 (s, 3H), 3.54 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 162.8, 162.6, 156.0, 154.9, 152.3, 150.4, 149.9, 149.6, 147.6, 145.5, 139.9 (3C), 139.3, 135.1, 134.2, 131.8, 129.2, 129.1, 128.5 (2C), 128.2, 124.7, 124.7, 123.9 (2C), 123.1, 122.0 (2C), 120.8, 118.9, 116.3, 115.5, 113.1, 112.1, 110.9, 108.4, 107.5, 106.3, 105.1, 94.1 (2C), 84.7 (2C), 56.3, 56.0, 55.9, 55.7. MS (ESI) m/z: 946 $(M+23)^+$, 924 $(M+1)^+$. Rf: 0.48 ($CH_2Cl_2$:EtOAc, 4:1).

Example 155: Compound **155**



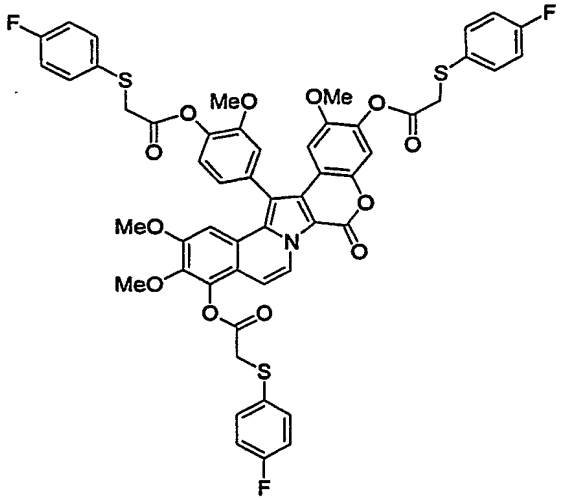
A suspension of **95** (21.0 mg, 0.0407 mmol), 5-(2-phenyleth-1-ynyl)nicotinic acid (36.3 mg, 0.1629 mmol), EDC·HCl (31.2 mg, 0.1629 mmol) and DMAP (7.0 mg, 0.0573 mmol) in $CH_2Cl_2$ (5 mL) was stirred at 23 °C for 2 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel ($CH_2Cl_2$:EtOAc, 4:1) to give **155** as a pale yellow solid (37.0 mg, 98%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$9.32 (br d, $J$= 1.9 Hz, 1H), 9.28 (br d, $J$= 1.9 Hz, 1H), 8.99-8.97 (m, 2H), 8.60 (t, $J$= 1.9 Hz, 1H), 8.6 (t, $J$= 1.9 Hz, 1H), 7.59-7.55 (m, 4H), 7.40-7.36 (m, 7H), 7.26-7.21 (m, 3H), 6.84 (s, 1H), 6.80 (s, 1H), 6.75 (s, 1H), 4.95-4.75 (m, 2H), 3.92 (s, 3H), 3.82 (s, 3H), 3.51 (s, 3H), 3.50 (s, 3H), 3.16 (t, $J$= 6.6 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$162.7, 156.0, 155.0, 152.1, 149.8, 149.2, 147.7, 147.6, 144.9, 139.9, 139.8, 139.6, 138.4, 135.9, 134.8, 131.7, 129.2, 129.1, 128.5, 128.5, 127.4, 126.5, 124.8 (2C), 123.7, 123.5, 122.0 (2C), 120.7, 119.6, 116.5, 115.0, 114.7, 114.5, 111.9, 111.0, 108.5, 105.6, 94.0, 93.9, 84.7 (2C), 56.2, 55.9, 55.8, 55.5, 42.5, 28.6. MS (ESI) m/z: 926 $(M+1)^+$. Rf: 0.48 ($CH_2Cl_2$:EtOAc, 4:1).

Example 156: Compound **156**



A suspension of **109** (50 mg, 0.0997 mmol), Boc-L-Ala-OH (75 mg, 0.3988 mmol), EDC·HCl (76 mg, 0.3988 mmol) and DMAP (7 mg, 0.0598 mmol) in $CH_2Cl_2$ (4.3 mL) was stirred under argon atmosphere at 23 °C for 2 h. The resulting pale yellow solution was washed with $H_2O$ (10 mL) and HCl 0.1 N (10 mL) and the aqueous phases were extracted with $CH_2Cl_2$ (10 mL). The organic phases were dried over anhydrous $Na_2SO_4$, filtered, and the solvent removed under vacuum. The residue was purified by chromatography on silica gel (hexane:EtOAc, from 2:1 to 1:1) to give **156** as a white solid (81 mg, 80%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.25-7.09 (m, 4H), 6.97 (s, 1H), 6.75 (d, $J$= 7.7 Hz, 1H), 6.67 (d, $J$= 10.1 Hz, 1H), 5.12 (br s, 2H), 4.89-4.85 (m, 1H), 4.70-4.55 (m, 3H), 3.78 (s, 3H), 3.40 (s, 3H), 3.33 (s, 3H), 2.03 (br t, 2H), 1.58 (d, $J$= 7.1 Hz, 3H), 1.52 (d, $J$= 7.1 Hz, 6H), 1.47 (s, 9H), 1.45 (s, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 171.4, 155.0, 152.0, 149.7, 147.4, 144.8, 139.7, 139.1, 138.6, 135.0, 134.1, 126.9, 126.8, 126.0, 125.9, 125.7, 123.7, 123.1, 122.4, 116.1, 115.8, 114.9, 114.7, 111.7, 109.6, 105.4, 79.9, 60.3, 56.1, 55.7, 55.7, 55.5, 55.4, 49.2, 42.3, 28.2, 27.9, 21.0, 18.5, 14.1. MS (ESI) m/z: 1037 $(M+23)^+$, 1015 $(M+1)^+$. Rf: 0.44 (hexane:EtOAc, 50:50).

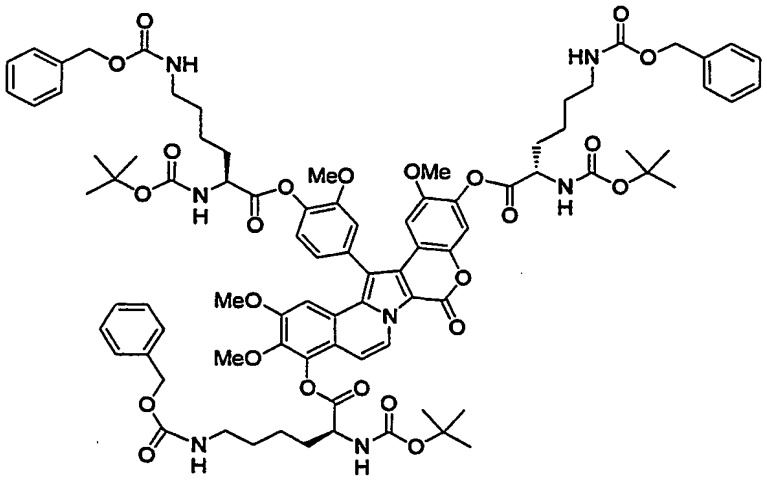
Example 157: Compound **157**



A suspension of **161** (27.3 mg, 0.0263 mmol) and DDQ (8.9 mg, 0.03952 mmol) in $CHCl_3$ (5 mL) was refluxed for 24 h under Argon atmosphere. The mixture was cooled

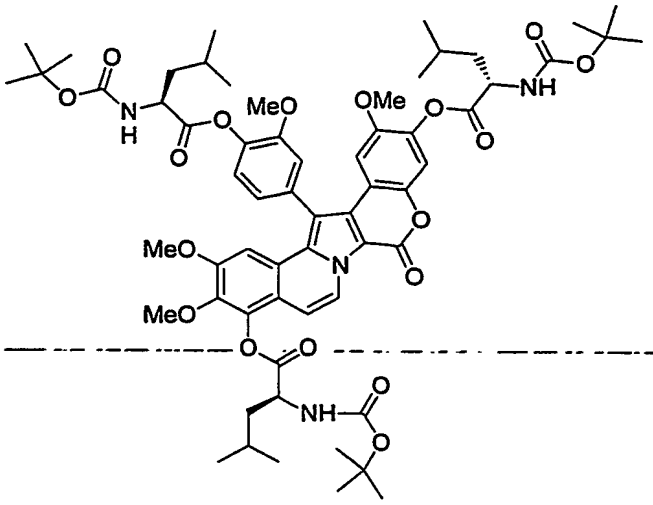
to 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (20 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, 60:40) to give **157** as a yellow solid (27.1 mg, quant.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.16 (d, $J$= 7.8 Hz, 1H), 7.60-7.50 (m, 6H), 7.22-7.20 (m, 1H), 7.10-7.00 (m, 10H), 6.75 (s, 2H), 3.93 (s, 2H), 3.87 (s, 2H), 3.82 (s, 3H), 3.80 (s, 2H), 3.79 (s, 3H), 3.45 (s, 3H), 3.37 (s, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 167.8, 167.7, 167.7, 164.6, 164.5, 161.3, 161.2, 155.1, 153.4, 152.5, 147.8, 145.6, 142.1, 140.3, 139.8, 138.9, 134.8, 134.1, 134.0, 133.4, 128.5, 124.0, 123.9, 123.7, 121.2, 118.3, 116.9, 116.6, 116.5, 116.4, 116.1, 115.4, 112.1, 115.4, 112.3, 112.2, 109.2, 106.7, 106.5, 104.5, 61.2, 56.5, 55.9, 55.8, 37.8. MS (ESI) m/z: 1034 $(M+1)^+$. Rf: 0.63 (hexane:EtOAc, 60:40).

Example 158: Compound **158**



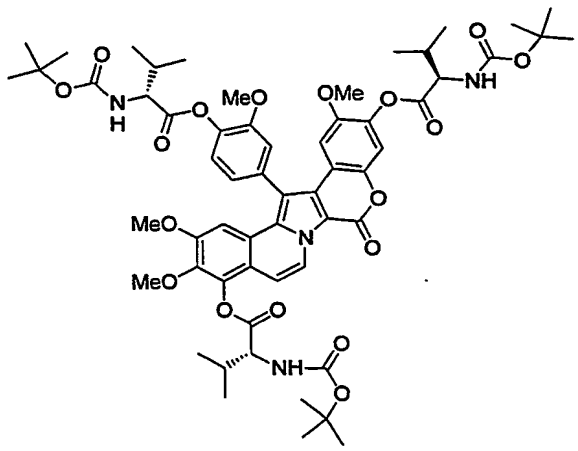
A suspension of **74** (71.5 mg, 0.0442 mmol) and DDQ (12.5 mg, 0.0552 mmol) in $CHCl_3$ (2.5 mL) was refluxed for 6 days under Argon atmosphere. The mixture was cooled to 23 °C then filtered through Celite, and washed with $CH_2Cl_2$ (20 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, 40:60) to give **158** as a yellow solid (48.3 mg, 68 %). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.20 (d, $J$= 7.5 Hz, 1H), 7.33-7.06 (m, 21H), 6.77 (d, $J$= 8.4 Hz, 1H), 5.09 (s, 6H), 4.94-4.91 (m, 3H), 4.56 (m, 3H), 3.85 (s, 3H), 3.79 (s, 3H), 3.48 (s, 3H), 3.41 (s, 3H), 3.25-3.24 (m, 6H), 2.19-1.82 (m, 6H), 1.62-11.50 (m, 12H), 1.46-1.45 (m, 27H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.5, 170.9 (2C), 156.8 (3C), 156.0, 155.7, 155.1, 153.3 (2C), 152.5, 147.8, 145.6 (2C), 141.9, 140.2, 139.6 (2C), 139.1 (2C), 136.2, 139.6 (2C), 139.1 (2C).136.8, 136.7, 134.8, 133.5 (2C), 128.8, 128.3, 124.3, 123.9, 123.7, 121.2, 118.5, 116.1, 115.4, 112.3, 109.2, 107.1, 106.4, 104.6, 80.6, 80.4 (2C), 66.9 (3C), 61.1, 56.5, 56.0 (2C), 54.0, 53.7 (2C), 40.8, 40.7 (2C), 32.3, 32.0 (2C), 29.8 (3C), 28.6 (9C), 22.6, 22.5 (2C). MS (ESI) m/z: 1638 $(M+23)^+$. Rf: 0.44 (hexane:EtOAc, 40:60).

Example 159: Compound **159**



A suspension of **76** (40.6 mg, 0.0347 mmol) and DDQ (9.8 mg, 0.0433 mmol) in $CHCl_3$ (2.5 mL) was refluxed for 6 days under Argon atmosphere. The mixture was cooled to 23 °C, filtered through Celite, and washed with $CH_2Cl_2$ (20 ml). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give **159** as a yellow solid (27.9 mg, 69 %). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.6 Hz, 1H), 7.32-7.08 (m, 6 H), 6.80-6.77 (m, 1 H), 5.01-4.98 (m, 3H), 6.60 (m, 3H), 3.84 (s, 3H), 3.81 (s, 3H), 3.48 (s, 3H), 3.43 (s, 3H), 1.91-1.62 (m, 9H), 1.50-1.46 (m, 27H), 1.06-0.99 (m, 18H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.9, 171.4, 155.6, 155.5, 155.3, 155.0, 153.2, 152.3, 147.6, 145.5, 145.4, 141.7, 140.1, 139.6, 139.0, 134.5, 133.2 (2C), 128.3, 124.0, 123.6, 123.5, 121.0, 118.4, 115.8, 115.1, 112.1, 109.0, 107.0, 106.2, 104.2, 80.4, 80.1 (2C), 56.2, 55.8, 55.7, 55.6, 52.6, 52.2 (2C), 41.7, 41.5, 41.3, 28.3 (9C), 24.8 (3C), 23.0, 22.9 (3C), 21.9, 21.8. MS (ESI) m/z: 1191 $(M+23)^+$. Rf: 0.55 (hexane:EtOAc, 2:1).

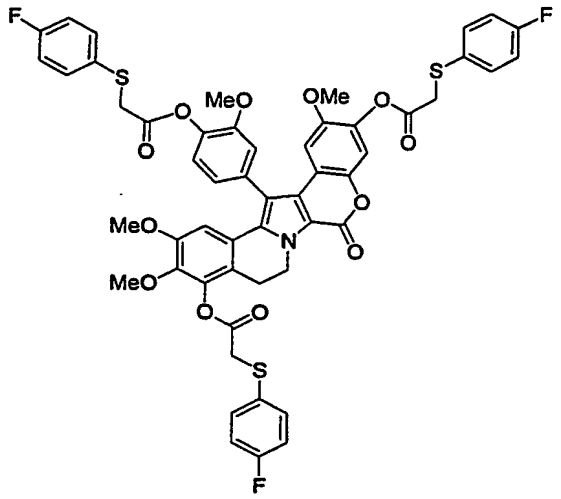
Example 160: Compound **160**



A suspension of **75** (48.3 mg, 0.042.7 mmol) and DDQ (12.1 mg, 0.0534 mmol) in $CHCl_3$ (2.5 mL) was refluxed for 3 days under Argon atmosphere. The mixture was cooled to 23 °C, filtered through Celite, and washed with $CH_2Cl_2$ (20 mL). The filtrated was concentrated under reduced pressure and the residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to give **160** as a yellow solid (37.8

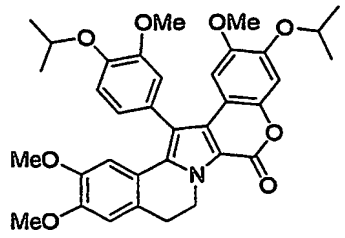
mg, 77%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 9.22 (d, $J$= 7.6 Hz, 1H), 7.33-7.09 (m, 6 H), 6.78 (d, $J$= 8.8 Hz, 1H), 5.12-5.06 (m, 3H), 4.63-4.53 (m, 3H); 3.86 (s, 3H), 3.81 (s, 3H), 3.49 (s, 3H), 3.43 (s, 3H), 2.46-2.35 (m, 3H), 1.49-1.44 (m, 27H), 1.31-1.01 (m, 18H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 170.4 (3C), 155.9, 155.7, 154.9, 153.11 (2C), 152.2, 147.6, 145.4 (2C), 141.7, 139.9, 138.7, 134.6, 133.2 (2C), 124.0, 123.6, 123.5, 121.0, 118.3, 115.8, 115.1, 112.1 (2C), 109.0, 106.9, 106.1, 104.2, 80.3, 79.9 (2C), 60.7, 59.0, 58.5 (2C), 56.0, 55.7, 55.6, 31.3, 31.1, 30.9, 28.3 (9C), 19.3, 19.2, 19.0, 17.5, 17.2, 17.1. MS (ESI) m/z: 1149 $(M+23)^+$, 1127 $(M+1)^+$. Rf: 0.42 (hexane:EtOAc, 2:1).

Example 161: Compound **161**



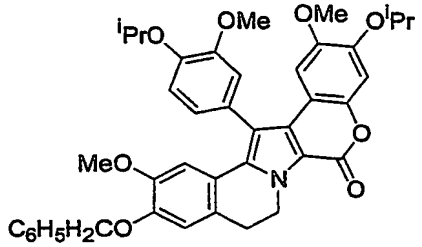

A suspension of **1** (50.0 mg, 0.094 mmol), 2-[(4-fluorophenyl)thio]acetic acid (105.0 mg, 0.564 mmol), EDC·HCl (108.2 mg, 0.564 mmol) and DMAP (1.0 mg, 0.008 mmol) in $CH_2Cl_2$ (2.5 mL) was stirred at 23 °C for 4 h under Argon atmosphere. The reaction mixture was washed with $H_2O$, dried over anhydrous $Na_2SO_4$, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:EtOAc, 3:2) to give a yellow solid which containing 2-[(4-fluorophenyl)thio]acetic acid. The solid was dissolved in $CH_2Cl_2$ (20 mL) and washed with 1 M NaOH (20 mL) to give **161** as a pale yellow solid (52.3 mg, 54 %). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.57-7.49 (m, 6H), 7.16-7.00 (m, 10H), 6.64 (s, 1H), 6.63 (s, 1H), 4.80-4.76 (m, 1H), 4.70-4.55 (m, 1H), 3.87 (s, 2H), 3.85 (s, 2H), 3.79 (s, 2H), 3.77 (s, 3H), 3.74 (s, 3H), 3.35 (s, 3H), 3.34 (s, 3H), 2.90 (br t, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 167.6, 167.5, 167.4, 164.2, 160.9, 154.8, 152.1, 151.8, 147.5, 144.8, 141.3, 141.1, 139.7, 138.6, 134.7, 134.3, 133.7 (2C), 133.6, 133.5, 133.4, 129.3 (2C), 126.9, 123.5, 123.2, 122.6, 119.0, 116.5, 116.3, 116.2, 116.1, 116.0, 115.6, 114.7, 111.6, 107.6, 105.5, 60.8, 56.2, 55.6, 55.4, 41.8, 37.5, 37.4, 37.3, 29.6. MS (ESI) m/z: 1057 $(M+23)^+$, 1035 $(M+1)^+$. Rf: 0.71 (hexane:EtOAc, 50:50).

Example 162: Compound **162**




6,7-Dimethoxy-3,4-dihydroisoquinoline (186.7 mg, 0.976 mmol) was added to a solution of LL-10 (479.7 mg, 0.976 mmol) in dry dimethylacetamide (20 mL) under Argon atmosphere. The solution was stirred at 23 °C for 24 h, then $Et_3N$ (150 µL, 1.07 mmol) was added and the reaction mixture was heated at 80 °C for 18 h. The solution was cooled to 23 °C, then $(KSO_3)_2NO$ (262.0 mg, 0.976 mmol) and saturated aqueous solution of $Na_2CO_3$ (3 mL) was added and the suspension was stirred for 1 h. After this time the mixture was treated with saturated aqueous solution of $NaHCO_3$ and extracted with $CH_2Cl_2$ (4x40 mL). The organic phases were dried over anhydrous $Na_2SO_4$ and the solvent was evaporated under reduced pressure. The resulted residue was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to afford 162 as a pale yellow solid (274.8 mg, 47%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.11-7.03 (m, 3H), 6.91 (s, 1H), 6.75 (s, 1H), 6.73 (s, 1H), 6.67 (s, 1H), 4.83-4.61 (m,2 H), 4.59-4.51 (m, 2H), 3.89 (s, 3H), 3.82 (s, 3H), 3.42, 3.36 (s, 3H), 3.12 (t, $J$= 6.8 Hz, 2H), 1.39-1.36 (m, 12H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.2, 152.0, 148.6, 147.1, 146.6, 146.1, 145.5, 135.5, 128.2, 127.8, 126.3, 123.1, 119.7, 116.6, 114.5, 114.4, 113.3, 110.7, 110.0, 108.3, 104.5, 103.0, 71.4, 71.0, 55.9, 55.6, 55.07, 54.7, 42.0, 28.3, 21.6, 21.5, 21.5, 21.4. MS (ESI) m/z: 600 $(M+1)^+$. Rf: 0.17 (hexane:EtOAc, 2:1).

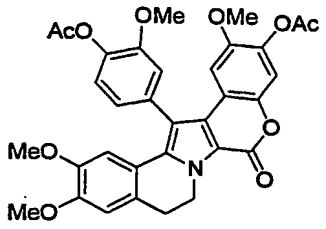
Example 163: Compound 163




6-Benzyloxy-7-methoxy-3,4-dihydroisoquinoline (50 mg, 0.187 mmol) was added to a solution of bromo-acetic acid 4-isopropoxy-2-(3-isopropoxy-4-methoxy-phenylethynyl)-5-methoxyphenyl ester (LL-10) (92 mg, 0.187 mmol) in anhydrous dimethylacetamide (5 mL) under Argon atmosphere. The solution was stirred at 23 °C for 23 h, then $Et_3N$ (29 µL, 0.205 mmol) was added and the reaction mixture was heated at 80 °C for 15 h. The solution was cooled, then $(KSO_3)_2NO$ (50 mg, 0.187 mmol) and saturated aqueous solution of $Na_2CO_3$ (1 mL) was added and the suspension was stirred at 23 °C for 1 h. After this time the mixture (pH 8) was extracted with $CH_2Cl_2$ (3x). The combined organic phases were dried over anhydrous $Na_2SO_4$ and the solvent was evaporated under reduced pressure. The residue obtained was purified by chromatography on silica gel (hexane:EtOAc, 2:1) to afford 163 as a pale yellow solid (42.5 mg, 34%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.43-7.29 (m, 5H), 7.09-7.03 (m, 3H), 6.90 (s, 1H), 6.76 (s, 1H), 6.75 (s, 1H), 6.66 (s, 1H), 5.14 (s, 2H), 4.79-4.50 (m, 4H), 3.82 (s, 3H), 3.42 (s, 3H), 3.37 (s, 3H), 3.04 (t, $J$= 6.8 Hz, 2H), 1.39-1.36 (m, 12H). $^{13}C$

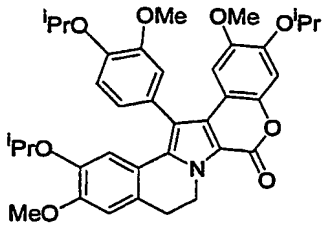
NMR (75 MHz, $CDCl_3$) $\delta$ 155.6, 151.2, 148.0, 148.0, 147.0, 146.9, 146.5, 145.9, 136.6, 135.8, 128.6, 128.5, 128.2, 128.0, 127.1, 126.4, 125.4, 123.4, 120.5, 116.9, 114.9, 114.5, 113.7, 113.3, 110.3, 109.0, 108.5, 104.8, 103.4, 71.7, 71.4, 70.9, 56.1, 55.4, 55.1, 42.3, 28.6, 21.8 (4C). MS (ESI) m/z: 676 $(M)^+$. Rf: 0.30 (hexane:EtOAc, 2:1).

Example 164: Compound **164**




A mixture of **95** (6.0 mg, 0.012 mmol) , $Ac_2O$ (0.75 mL) and pyridine (1.5 mL) was stirred at 23 °C for 20 h under Argon atmosphere. The solvent was evaporated under reduced pressure to give **164** as a brown solid (7 mg, quant.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.23-7.09 (m, 4 H), 6.76 (s, 1H), 6.72 (s, 1H), 6.69 (s, 1H), 4.90-4.74 (m, 2H), 4.30 (t, $J$= 6.6 Hz, 2H), 3.90 (s, 3H), 3.80 (s, 3H), 3.43 (s, 3H), 3.16 (s, 3H), 3.14 (t, $J$= 6.6 Hz, 2H), 2.34 (s, 3H), 2.31 (s, 2H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 168.7, 152.14, 149.14, 147.7 (2C), 139.9, 138.8, 134.3, 130.9, 128.8, 126.4, 126.3, 123.8, 123.3, 119.7, 116.2, 114.8 (2C), 111.9, 111.0, 108.5, 105.5, 56.2, 55.9, 55.7, 55.4, 42.5, 29.7 (2C), 29.4 MS (ESI) m/z: 600 $(M+1)^+$. Rf: 0.27 (EtOAc:hexane, 2:1).

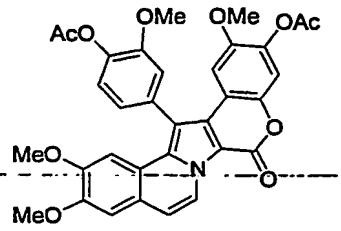
Example 165: Compound **165**




7-Isopropoxy-6-methoxy-3,4-dihydroisoquinoline (284.5 mg, 0.5791 mmol) was added to a solution of LL-10 (127.0 mg, 0.5891 mmol) in dry dimethylacetamide (4 mL) under Argon atmosphere. The solution was stirred at 23 °C for 15 h, then $Et_3N$ (89 µL, 0.637 mmol) was added and the reaction mixture was heated at 80 °C for 19 h. The solution was cooled to 23 °C, then $(KSO_3)_2NO$ (155.4 mg, 0.5791 mmol) and saturated aqueous solution of $Na_2CO_3$ (1 mL) was added and the suspension was stirred for 1 h. After this time the mixture was treated with saturated aqueous solution of $NaHCO_3$ and extracted with $CH_2Cl_2$. The combined organic layers were dried over anhydrous $Na_2SO_4$ and the solvent was evaporated under reduced pressure. The resulted residue was purified by chromatography on silica gel (hexane-EtOAc, 50:50) to afford **165** as a pale yellow solid (84.6 mg, 23%). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.08-7.00 (m, 3H), 6.86 (s, 1H), 6.74 (s, 2H), 6.60 (s, 1H), 4.78-4.71 (m, 2H), 4.60-4.41 (m, 2H), 3.88-3.77 (m, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.40 (s, 3H), 3.08 (t, $J$= 6.8 Hz, 2H), 1.40 (d, $J$= 6.1 Hz, 6H), 1.33 (d, $J$= 6.0 Hz, 6H), 1.10 (d, $J$= 6.1 Hz, 3H), 1.07 (d, $J$= 6.1 Hz, 3H). $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 155.5, 151.1, 149.9, 147.0, 146.8, 146.4, 145.8, 145.7, 135.8, 128.3, 128.2, 126.4, 123.2, 119.9, 116.2, 114.7, 114.3, 113.5, 111.9, 111.4, 110.3, 104.8,

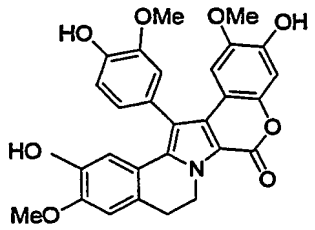
103.3, 71.5, 71.3, 70.7, 55.9, 55.8, 55.3, 42.3, 28.6, 21.9, 21.8, 21.7, 21.5(2C), 20.9. MS (ESI) m/z: 650 $(M+23)^+$, 628 $(M+1)^+$. Rf: 0.41 (hexane:EtOAc, 50:50).

Example 166: Compound **166**




A mixture of **26** (6.0 mg, 0.012 mmol), $Ac_2O$ (0.75 mL) and pyridine (1.5 mL) was stirred at 23 °C for 20 h under Argon atmosphere. The solvent was evaporated under reduced pressure to give a brown solid which was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to afford **166** (7 mg, quant.). $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.30 (d, $J$= 7.6 Hz, 1H), 7.31-7.26 (m, 5H), 7.23-7.10 (m, 2H), 6.84 (s, 1H), 4.00 (s, 3H), 3.83 (s, 3H), 3.51 (s,3H), 3.46 (s, 3H), 2.37 (s, 2H), 2.32 (s, 2H). MS (ESI) m/z: 620 $(M+23)^+$, 598 $(M+1)^+$. Rf: 0.60 ($CH_2Cl_2$:MeOH, 10:1).

Example 167: Compound **167**




A suspension of **165** (80.4 mg, 0.128 mmol) and $AlCl_3$ (51.2 mg, 0.384 mmol) in anhydrous $CH_2Cl_2$ (4 mL) was stirred from 0 °C to 23 °C for 1 h under Argon atmosphere. MeOH (1 mL) was added and the solvent was evaporated under reduced pressure. The brown residue was purified by chromatography on silica gel ($CH_2Cl_2$:MeOH, 20:1) to afford **167** as a beige solid (35.3 mg, 55%). $^1H$ NMR (300 MHz, DMSO-$d_6$) $\delta$ 9.66 (br s, 1H), 9.26 (br s, 1H), 8.85 (br s, 1H), 6.99-6.94 (m, 3H), 6.83 (dd, $J$= 7.8, 1.7 Hz, 1H), 6.78 (s, 1H), 6.66 (s 1H), 6.46 (s, 1H), 4.62 (br t, $J$= 5.9 Hz, 2H), 3.79 (s, 3H), 3.73 (s, 3H), 3.33 (s, 3H), 3.06 (br t, $J$= 5.9 Hz, 2H). $^{13}C$ NMR (75 MHz, DMSO-$d_6$) $\delta$ 154.3, 148.4, 148.0, 146.8, 146.5, 145.6, 144.8, 144.4, 135.4, 127.9, 125.5, 125.3, 123.3, 119.7, 116.4, 114.8, 114.5, 112.8, 112.4, 111.9, 108.8, 105.0, 103.5, 55.9, 55.6, 55.0, 42.0, 28.0. MS (ESI) m/z: 524 $(M+23)^+$, 502 $(M+1)^+$. Rf: 0.25 ($CH_2Cl_2$:MeOH, 20:1).

## CYTOTOXICITY

### BIOASSAYS FOR ANTITUMOR SCREENING

The finality of these assays is to interrupt the growth of a "in vitro" tumor cell culture by means a continued exhibition of the cells to the sample to be testing.

### CELL LINES

| Name | N° ATCC | Species | Tissue | Characteristics |
|---|---|---|---|---|
| P-388 | CCL-46 | mouse | ascites fluid | lymphoid neoplasm |
| K-562 | CCL-243 | human | leukemia | erythroleukemia (pleural effusion) |
| A-549 | CCL-185 | human | lung | lung carcinoma "NSCL" |
| SK-MEL-28 | HTB-72 | human | melanoma | malignant melanoma |
| HT-29 | HTB-38 | human | colon | colon adenocarcinoma |
| LoVo | CCL-229 | human | colon | colon adenocarcinoma |
| LoVo-Dox | | human | colon | colon adenocarcinoma (MDR) |
| SW620 | CCL-228 | human | colon | colon adenocarcinoma (lymph node metastasis) |
| DU-145 | HTB-81 | human | prostate | prostate carcinoma, not androgen receptors |
| LNCaP | CRL-1740 | human | prostate | prostate adenocarcinoma, with androgen receptors |
| SK-BR-3 | HTB-30 | human | breast | breast adenocarcinoma, Her2/neu+, (pleural effusion) |
| MCF-7 | HTB-22 | human | breast | breast adenocarcinoma, (pleural effusion) |
| MDA-MB-231 | HTB -26 | human | breast | breast adenocarcinoma, Her2/neu+, (pleural effusion) |
| IGROV-1 | | human | ovary | ovary adenocarcinoma |
| IGROV-ET | | human | ovary | ovary adenocarcinoma, characterized as ET-743 resistant cells |

| | | | | |
|---|---|---|---|---|
| SK-OV-3 | HTB-77 | human | ovary | ovary adenocarcinoma (malignant ascites) |
| OVCAR-3 | HTB-161 | human | ovary | ovary adenocarcinoma |
| HeLa | CCL-2 | human | cervix | cervix epitheloid carcinoma |
| HeLa-APL | CCL-3 | human | cervix | cervix epitheloid carcinoma, characterized as aplidine resistant cells |
| A-498 | HTB-44 | human | kidney | kidney carcinoma |
| PANC-1 | CRL-1469 | human | pancreas | pancreatic epitheloid carcinoma |
| HMEC1 | | human | endothelium | |

Inhibition of cells growth by colorimetric assay.

A colorimetric type of assay, using sulforhodamine B (SRB) reaction has been adapted for a quantitative measurement of cell growth and viability [following the technique described by Philip Skehan, et al. (1990), New colorimetric cytotoxicity assay for anticancer drug screening, *J. Natl. Cancer Inst.*, 82:1107-1112]

This form of the assay employs 96 well cell culture microplates of 9 mm diameter (Faircloth, 1988; Mosmann, 1983). Most of the cell lines are obtained from American Type Culture Collection (ATCC) derived from different human cancer types.

Cells are maintained in RPMI 1640 10% FBS, supplemented with 0.1 g/l penicillin and 0.1 g/l streptomycin sulfate and then incubated at 37°C, 5% $CO_2$ and 98% humidity. For the experiments, cells were harvested from subconfluent cultures using trypsin and resuspended in fresh medium before plating.

Cells are seeded in 96 well microtiter plates, at 5 x $10^3$ cells per well in aliquots of 195 µl medium, and they are allowed to attach to the plate surface by growing in drug free medium for 18 hours. Afterward,

samples are added in aliquots of 5 µl in a ranging from 10 to $10^{-8}$ µg/ml, dissolved in DMSO/EtOH/PBS (0.5:0.5:99). After 48 hours exposure, the antitumor effect are measured by the SRB methodology: cells are fixed by adding 50 µl of cold 50% (wt/vol) trichloroacetic acid (TCA) and incubating for 60 minutes at 4°C. Plates are washed with deionized water and dried. One hundred µl of SRB solution (0.4% wt/vol in 1% acetic acid) is added to each microtiter well and incubated for 10 minutes at room temperature. Unbound SRB is removed by washing with 1% acetic acid. Plates are air dried and bound stain is solubilized with Tris buffer. Optical densities are read on a automated spectrophotometric plate reader at a single wavelength of 490 nm.

The values for mean +/- SD of data from triplicate wells are calculated. Some parameters for cellular responses can be calculated: GI = growth inhibition, TGI = total growth inhibition (cytostatic effect) and LC = cell killing (cytotoxic effect).

Obtained results may predict the usefulness of a certain drug as a potential cancer treatment. For this technique, compounds which show GI50 values smaller than 10 µg/ml are selected to continue with further studies. GI50's data allow to predict that not only could a drug be cystostatic, but also it could have a potential in terms of tumor reduction.

Activity Data (Molar)

| | | 1 | 2 | 2 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 6.40E-08 | 8.24E-06 | 1.90E-08 | 2.18E-07 | 3.56E-08 | 3.55E-07 | 9.93E-07 | 7.03E-07 | 5.43E-08 | 8.44E-07 | 3.53E-08 | 2.49E-07 |
| | TGI | 1.40E-07 | 1.18E-05 | 7.97E-08 | 6.67E-07 | 1.19E-07 | 1.46E-06 | 2.31E-06 | 2.60E-06 | 1.69E-07 | 9.17E-06 | 1.51E-07 | 1.43E-06 |
| | LC50 | 1.89E-05 | 1.70E-05 | 2.00E-05 | 2.14E-06 | 5.75E-07 | 7.96E-06 | 5.41E-06 | 9.43E-06 | 6.15E-07 | 9.17E-06 | 2.78E-06 | 7.07E-06 |
| LN-caP | GI50 | 7.27E-08 | 2.77E-07 | 1.23E-07 | 3.32E-07 | 2.23E-07 | 5.78E-07 | 4.25E-07 | 6.54E-07 | 1.74E-07 | 1.34E-06 | - | - |
| | TGI | 3.98E-07 | 1.44E-06 | 3.98E-07 | 7.85E-07 | 1.05E-06 | 7.96E-06 | 1.36E-06 | 2.47E-06 | 4.22E-07 | 3.65E-06 | - | - |
| | LC50 | 1.44E-06 | 7.85E-06 | 1.06E-06 | 1.85E-06 | 3.62E-06 | 7.96E-06 | 3.61E-06 | 7.21E-06 | 1.38E-06 | 9.17E-06 | - | - |
| SKOV-3 | GI50 | 1.40E-07 | 1.37E-05 | 5.37E-08 | - | - | - | - | - | - | - | - | - |
| | TGI | 5.10E-06 | 1.88E-05 | 2.40E-07 | - | - | - | - | - | - | - | - | - |
| | LC50 | 1.89E-05 | 1.88E-05 | 1.58E-05 | - | - | - | - | - | - | - | - | - |
| IGROV | GI50 | 8.80E-07 | 4.93E-07 | 2.36E-07 | 4.02E-07 | 2.47E-07 | 9.63E-07 | 1.23E-06 | 4.45E-07 | 1.82E-07 | 5.56E-07 | 2.67E-07 | 1.42E-06 |
| | TGI | 5.17E-06 | 1.76E-06 | 1.06E-06 | 2.00E-06 | 8.55E-07 | 7.96E-06 | 2.67E-06 | 2.17E-06 | 9.09E-07 | 9.17E-06 | 1.14E-06 | 3.38E-06 |
| | LC50 | 1.89E-05 | 1.88E-05 | 2.00E-05 | 1.13E-05 | 4.54E-06 | 7.96E-06 | 5.79E-06 | 1.12E-05 | 3.00E-06 | 9.17E-06 | 5.88E-06 | 8.01E-06 |
| IGROV-ET | GI50 | 1.98E-06 | 4.44E-07 | 2.14E-07 | 5.99E-07 | 2.12E-07 | 1.39E-06 | 1.86E-06 | 3.35E-06 | 1.32E-07 | 2.57E-06 | 5.53E-06 | 1.09E-05 |
| | TGI | 8.12E-06 | 1.20E-06 | 1.16E-06 | 1.64E-06 | 1.06E-06 | 7.96E-06 | 4.58E-06 | 1.12E-05 | 9.80E-07 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| | LC50 | 1.89E-05 | 1.88E-05 | 2.00E-05 | 1.31E-05 | 6.09E-06 | 7.96E-06 | 8.14E-06 | 1.12E-05 | 4.93E-07 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| SK-BR-3 | GI50 | 3.14E-07 | 2.37E-06 | 1.06E-07 | 3.38E-07 | 2.41E-07 | 5.48E-07 | 1.14E-06 | 9.15E-07 | 1.74E-07 | 1.23E-06 | 1.87E-07 | 6.98E-07 |
| | TGI | 2.36E-06 | 1.09E-05 | 7.67E-07 | 7.03E-07 | 5.95E-07 | 2.56E-06 | 2.61E-06 | 3.04E-06 | 3.74E-07 | 6.59E-06 | 1.20E-06 | 3.45E-06 |
| | LC50 | 1.88E-05 | 1.88E-05 | 7.69E-06 | 1.47E-06 | 3.54E-06 | 7.96E-06 | 5.98E-06 | 9.19E-06 | 8.06E-07 | 9.17E-06 | 6.66E-06 | 1.09E-05 |
| MEL-28 | GI50 | 3.02E-07 | 2.24E-06 | 8.81E-08 | - | 6.29E-08 | 3.86E-07 | 6.52E-07 | 4.07E-07 | 1.34E-07 | 2.14E-06 | 2.00E-07 | 1.77E-06 |
| | TGI | 3.66E-06 | 5.04E-06 | 1.77E-06 | - | 2.49E-07 | 1.74E-06 | 1.64E-06 | 2.20E-06 | 5.16E-07 | 9.17E-06 | 1.18E-06 | 5.98E-06 |
| | LC50 | 1.89E-05 | 1.13E-05 | 1.13E-05 | - | 1.12E-06 | 7.96E-06 | 3.75E-06 | 1.12E-05 | 2.11E-06 | 9.17E-06 | 6.18E-06 | 1.09E-05 |
| H-MEC-1 | GI50 | 6.65E-07 | 6.06E-07 | 1.13E-07 | - | - | - | - | - | - | - | - | - |
| | TGI | 1.89E-05 | 1.38E-06 | 3.14E-06 | - | - | - | - | - | - | - | - | - |
| | LC50 | 1.89E-05 | 5.72E-06 | 1.55E-05 | - | - | - | - | - | - | - | - | - |
| A-549 | GI50 | 6.74E-07 | 1.88E-06 | 2.04E-08 | 5.43E-07 | 1.21E-07 | 4.97E-07 | 9.69E-07 | 7.44E-07 | 3.23E-07 | 4.33E-06 | 1.28E-07 | 1.20E-06 |
| | TGI | 1.89E-05 | 1.88E-06 | 1.14E-06 | 1.21E-06 | 1.02E-06 | 7.96E-06 | 2.96E-06 | 6.34E-06 | 1.15E-06 | 9.17E-06 | 1.54E-06 | 6.64E-06 |
| | LC50 | 1.89E-05 | 1.88E-06 | 1.55E-05 | 1.00E-05 | 4.65E-06 | 7.96E-06 | 8.14E-06 | 1.12E-05 | 6.76E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| K-562 | GI50 | 1.17E-07 | 8.15E-07 | 8.69E-08 | 3.96E-07 | 7.70E-08 | 4.82E-07 | 5.96E-07 | 2.25E-07 | 4.73E-08 | 9.53E-07 | - | - |
| | TGI | 2.25E-06 | 2.11E-06 | 7.91E-07 | 9.37E-07 | 1.10E-06 | 5.38E-06 | 2.68E-06 | 1.57E-06 | 3.11E-07 | 9.17E-06 | - | - |
| | LC50 | 1.89E-05 | 2.97E-06 | 8.15E-06 | 4.44E-06 | 7.40E-06 | 7.96E-06 | 8.14E-06 | 7.49E-06 | 4.18E-06 | 9.17E-06 | - | - |
| PANC-1 | GI50 | 9.88E-07 | 2.20E-06 | 2.48E-07 | 4.80E-07 | 4.18E-07 | 2.46E-06 | 1.36E-06 | 2.31E-07 | 2.00E-07 | 1.09E-06 | 2.14E-07 | 1.62E-06 |
| | TGI | 6.97E-06 | 7.94E-06 | 2.20E-06 | 1.34E-06 | 1.64E-06 | 7.96E-06 | 3.31E-06 | 8.65E-07 | 1.56E-06 | 4.49E-06 | 1.76E-06 | 8.94E-06 |
| | LC50 | 1.89E-05 | 1.88E-05 | 2.00E-05 | 5.99E-06 | 4.51E-06 | 7.96E-06 | 8.04E-06 | 1.12E-05 | 4.91E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| HT-29 | GI50 | 8.31E-06 | 1.88E-05 | 5.33E-06 | 2.50E-06 | 1.70E-06 | 7.96E-06 | 8.71E-07 | 3.77E-07 | 1.61E-06 | 3.89E-06 | 3.84E-08 | 8.11E-08 |
| | TGI | 1.89E-05 | 1.88E-05 | 1.90E-05 | 6.03E-06 | 3.24E-06 | 7.96E-06 | 3.31E-06 | 1.12E-05 | 3.28E-06 | 9.17E-06 | 1.75E-07 | 8.41E-07 |
| | LC50 | 1.89E-05 | 1.88E-05 | 2.00E-05 | 1.46E-05 | 6.16E-06 | 7.96E-06 | 8.14E-06 | 1.12E-05 | 6.66E-06 | 9.17E-06 | 8.23E-06 | 1.09E-05 |
| LOVO | GI50 | 3.98E-07 | 1.18E-05 | 3.98E-07 | 4.68E-07 | 3.45E-07 | 2.79E-06 | 2.00E-06 | 1.48E-06 | 2.43E-07 | 2.07E-06 | 4.24E-08 | 1.83E-06 |
| | TGI | 3.02E-06 | 5.76E-05 | 9.65E-07 | 1.08E-06 | 1.06E-06 | 7.96E-06 | 5.05E-06 | 4.68E-06 | 5.84E-07 | 5.47E-06 | 1.16E-06 | 7.41E-06 |
| | LC50 | 1.60E-05 | 1.88E-05 | 2.00E-06 | 4.36E-06 | 4.14E-06 | 7.96E-06 | 8.14E-06 | 1.12E-05 | 2.30E-06 | 9.17E-06 | 1.04E-05 | 1.09E-05 |
| LOVO-DOX | GI50 | 6.04E-07 | 8.01E-07 | 4.20E-07 | 2.00E-06 | 4.09E-07 | 3.84E-06 | 3.66E-06 | 8.34E-06 | 3.88E-07 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| | TGI | 3.83E-06 | 7.13E-06 | 1.67E-06 | 5.95E-06 | 1.10E-06 | 7.96E-06 | 8.14E-06 | 1.12E-05 | 1.14E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| | LC50 | 1.89E-05 | 1.88E-05 | 2.00E-05 | 1.78E-05 | 3.40E-06 | 7.96E-06 | 8.14E-06 | 1.12E-05 | 3.63E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| HELA | GI50 | - | - | - | 3.38E-07 | 1.24E-07 | 5.84E-07 | 8.30E-07 | 2.76E-07 | 1.07E-07 | 1.20E-06 | 2.08E-07 | 1.66E-06 |
| | TGI | - | - | - | 6.85E-07 | 1.12E-06 | 7.96E-06 | 1.91E-06 | 1.41E-06 | 4.59E-07 | 4.37E-06 | 1.35E-06 | 7.50E-06 |
| | LC50 | - | - | - | 1.39E-06 | 3.10E-06 | 7.96E-06 | 4.42E-06 | 7.92E-06 | 4.06E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| HELA-APL | GI50 | - | - | - | 2.38E-07 | 3.10E-07 | 3.41E-06 | 1.85E-06 | 7.30E-06 | 2.82E-07 | 3.42E-06 | 5.23E-06 | 3.66E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | - | - | - | 6.81E-07 | 1.71E-06 | 7.96E-06 | 3.66E-06 | 1.12E-05 | 1.23E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |
| | LC50 | - | - | - | 1.95E-06 | 5.55E-06 | 7.96E-06 | 7.24E-06 | 1.12E-05 | 3.83E-06 | 9.17E-06 | 1.11E-05 | 1.09E-05 |

| | | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 8.32E-07 | 5.17E-07 | 6.85E-08 | 5.27E-08 | 4.87E-08 | 5.05E-07 | 5.32E-07 | 5.00E-07 | 3.53E-07 | 7.43E-07 | 1.76E-07 |
| | TGI | 3.64E-06 | 2.19E-06 | 3.08E-06 | 2.98E-07 | 2.28E-07 | 1.41E-06 | 2.16E-06 | 2.36E-06 | 7.03E-07 | 8.10E-06 | 1.62E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 1.10E-05 | 2.80E-06 | 2.30E-06 | 7.04E-06 | 6.85E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| LN-caP | GI50 | - | - | 5.60E-08 | 1.31E-07 | 1.32E-07 | 3.59E-07 | 9.41E-08 | - | 1.90E-07 | 5.64E-07 | 1.68E-07 |
| | TGI | - | - | 6.09E-07 | 2.65E-07 | 2.81E-07 | 1.27E-06 | 1.41E-06 | - | 3.83E-07 | 1.82E-06 | 5.34E-07 |
| | LC50 | - | - | 3.93E-06 | 5.34E-07 | 5.99E-07 | 4.27E-06 | 5.37E-06 | - | 7.75E-07 | 1.36E-05 | 2.34E-06 |
| SKOV-3 | GI50 | - | - | - | - | - | 1.22E-06 | 7.58E-07 | - | 8.49E-07 | 2.01E-07 | 1.18E-08 |
| | TGI | - | - | - | - | - | 2.82E-06 | 2.31E-06 | - | 1.17E-05 | 2.22E-06 | 3.20E-07 |
| | LC50 | - | - | - | - | - | 6.51E-06 | 6.57E-06 | - | 1.17E-05 | 1.36E-05 | 1.97E-06 |
| IGROV | GI50 | 1.29E-06 | 4.90E-07 | 8.62E-08 | 2.26E-07 | 1.05E-07 | 1.31E-06 | 4.06E-07 | 5.16E-07 | 3.15E-07 | 7.87E-07 | 3.30E-07 |
| | TGI | 4.79E-06 | 2.44E-06 | 2.03E-06 | 4.78E-07 | 4.05E-07 | 3.21E-06 | 2.51E-06 | 7.46E-06 | 6.64E-07 | 8.54E-06 | 1.92E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 9.76E-06 | 1.59E-06 | 4.93E-06 | 7.91E-06 | 9.34E-06 | 1.53E-05 | 9.02E-06 | 1.36E-05 | 5.82E-06 |
| IGROV-ET | GI50 | 1.96E-06 | 7.45E-07 | 6.87E-06 | 2.78E-07 | 1.62E-07 | 2.00E-06 | 7.61E-07 | 5.93E-07 | 9.01E-07 | 2.89E-06 | 1.86E-06 |
| | TGI | 7.86E-06 | 4.97E-06 | 1.10E-05 | 5.00E-07 | 5.44E-07 | 5.14E-06 | 2.54E-06 | 1.53E-05 | 5.18E-06 | 1.36E-05 | 5.82E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 1.10E-05 | 8.97E-07 | 8.78E-06 | 1.23E-05 | 1.13E-05 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| SK-BR-3 | GI50 | 4.54E-08 | 4.24E-08 | 5.61E-08 | 2.07E-07 | 8.03E-08 | 4.58E-07 | 1.65E-07 | 5.48E-08 | 3.42E-07 | 2.57E-07 | 3.91E-08 |
| | TGI | 1.13E-07 | 9.88E-08 | 6.35E-07 | 4.11E-07 | 2.86E-07 | 2.14E-06 | 2.28E-06 | 2.38E-07 | 5.99E-07 | 1.81E-06 | 3.03E-07 |
| | LC50 | 1.02E-05 | 1.40E-05 | 5.84E-06 | 8.16E-07 | 1.22E-06 | 1.05E-05 | 1.40E-05 | 1.53E-05 | 1.17E-05 | 7.16E-06 | 2.85E-06 |
| MEL-28 | GI50 | 3.11E-06 | 1.42E-06 | 4.82E-08 | 1.38E-07 | 5.18E-08 | 5.24E-07 | 2.73E-07 | 2.24E-06 | 2.87E-07 | 3.32E-07 | 6.99E-08 |
| | TGI | 1.09E-05 | 1.40E-05 | 1.64E-06 | 3.04E-07 | 1.71E-07 | 1.44E-06 | 1.53E-06 | 1.53E-05 | 4.97E-07 | 3.56E-06 | 8.15E-07 |
| | LC50 | 1.24E-05 | 1.40E-05 | 7.24E-06 | 6.69E-07 | 7.66E-07 | 4.43E-06 | 4.99E-06 | 1.53E-05 | 8.60E-07 | 1.36E-05 | 3.09E-06 |
| H-MEC-1 | GI50 | - | - | - | - | - | 4.94E-07 | 8.07E-07 | - | 2.81E-07 | 8.56E-07 | 2.19E-07 |
| | TGI | - | - | - | - | - | 8.46E-07 | 2.42E-06 | - | 5.09E-07 | 2.91E-06 | 6.87E-07 |
| | LC50 | - | - | - | - | - | 2.93E-06 | 7.16E-06 | - | 9.22E-07 | 1.04E-05 | 2.87E-06 |
| A-549 | GI50 | 9.06E-07 | 5.55E-07 | 5.41E-08 | 1.78E-07 | 2.07E-07 | 1.61E-06 | 6.05E-07 | 5.89E-07 | 1.39E-06 | 8.90E-07 | 2.43E-07 |
| | TGI | 1.24E-05 | 1.40E-05 | 1.46E-06 | 5.02E-07 | 6.63E-07 | 4.00E-06 | 2.13E-06 | 1.53E-05 | 4.62E-06 | 7.73E-06 | 3.24E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 1.10E-05 | 3.05E-06 | 8.48E-06 | 9.99E-06 | 6.32E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| K-562 | GI50 | - | - | 1.60E-06 | 1.83E-07 | 5.36E-08 | 5.58E-07 | 1.84E-06 | - | 2.86E-07 | 6.70E-07 | 2.48E-07 |
| | TGI | - | - | 3.91E-06 | 4.45E-07 | 2.77E-07 | 1.51E-06 | 4.62E-06 | - | 5.82E-07 | 4.77E-06 | 1.01E-06 |
| | LC50 | - | - | 9.57E-06 | 2.23E-06 | 2.50E-06 | 8.64E-06 | 1.16E-05 | - | 2.39E-06 | 1.36E-05 | 3.36E-06 |
| PANC-1 | GI50 | 2.43E-06 | 1.18E-06 | 1.54E-06 | 2.41E-07 | 2.06E-07 | 9.92E-07 | 2.45E-07 | 1.24E-06 | 5.14E-07 | 9.76E-07 | 4.20E-07 |
| | TGI | 1.24E-05 | 1.40E-05 | 5.26E-06 | 7.56E-07 | 1.52E-06 | 3.70E-06 | 2.42E-06 | 1.53E-05 | 1.81E-06 | 1.36E-05 | 3.33E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 1.10E-05 | 3.34E-06 | 8.53E-06 | 1.23E-05 | 9.50E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| HT-29 | GI50 | 3.22E-06 | 2.47E-06 | 4.73E-08 | 4.11E-07 | 3.42E-07 | 8.19E-07 | 1.09E-07 | 3.58E-06 | 5.12E-07 | 8.79E-07 | 2.90E-07 |
| | TGI | 6.39E-06 | 7.26E-06 | 1.11E-07 | 9.31E-07 | 6.86E-07 | 4.54E-06 | 2.10E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 9.17E-06 | 5.00E-06 | 8.78E-06 | 1.23E-05 | 7.29E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| LOVO | GI50 | 7.54E-07 | 5.97E-07 | 1.68E-06 | 1.96E-07 | 2.16E-07 | 6.64E-07 | 7.22E-07 | 4.36E-07 | 1.95E-06 | 4.84E-07 | 2.02E-07 |
| | TGI | 2.35E-06 | 2.47E-06 | 4.96E-06 | 3.47E-07 | 4.20E-07 | 2.37E-06 | 2.33E-06 | 5.83E-06 | 4.97E-06 | 2.49E-06 | 1.40E-06 |
| | LC50 | 9.02E-06 | 1.40E-05 | 1.10E-05 | 6.12E-07 | 8.16E-07 | 1.23E-05 | 6.60E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| LOVO-DOX | GI50 | 6.75E-07 | 4.97E-07 | 1.10E-05 | 4.20E-07 | 3.84E-07 | 1.08E-06 | 8.74E-07 | 5.25E-07 | 4.97E-06 | 6.59E-06 | 1.61E-06 |
| | TGI | 3.42E-06 | 1.45E-06 | 1.10E-05 | 1.03E-06 | 1.33E-06 | 3.67E-06 | 2.72E-06 | 2.06E-06 | 1.17E-05 | 1.36E-05 | 4.70E-06 |
| | LC50 | 1.24E-05 | 1.40E-05 | 1.10E-05 | 4.42E-06 | 5.29E-06 | 1.21E-05 | 8.03E-06 | 1.53E-05 | 1.17E-05 | 1.36E-05 | 5.82E-06 |
| HELA | GI50 | 1.83E-06 | 1.83E-06 | 5.79E-08 | 1.93E-07 | 1.09E-07 | - | - | 1.17E-06 | - | - | - |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 9.63E-06 | 9.63E-06 | 1.41E-06 | 3.68E-07 | 3.59E-07 | - | - | 1.53E-05 | - | - | - |
| | LC50 | 1.24E-05 | 1.24E-05 | 7.81E-06 | 7.03E-07 | 8.78E-07 | - | - | 1.53E-05 | - | - | - |
| HELA-APL | GI50 | 2.60E-06 | 2.60E-06 | 2.43E-06 | 2.29E-07 | 1.19E-07 | - | - | 2.09E-06 | - | - | - |
| | TGI | 1.21E-05 | 1.21E-05 | 5.53E-06 | 5.20E-07 | 3.53E-07 | - | - | 1.53E-05 | - | - | - |
| | LC50 | 1.24E-05 | 1.24E-05 | 1.10E-05 | 2.38E-06 | 1.85E-06 | - | - | 1.53E-05 | - | - | - |

| | | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 9.13E-07 | 2.52E-08 | 6.11E-07 | 9.76E-07 | 3.15E-07 | 1.98E-07 | 5.38E-08 | 3.01E-07 | 1.11E-07 | 1.86E-08 | 1.96E-07 |
| | TGI | 2.94E-06 | 1.01E-07 | 2.94E-06 | 3.95E-06 | 1.47E-06 | 4.40E-07 | 2.65E-07 | 8.61E-07 | 3.09E-07 | 4.60E-08 | 5.88E-07 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.95E-05 | 1.26E-05 | 7.32E-06 | 3.90E-06 | 3.84E-06 | 7.62E-06 | 8.57E-07 | 3.67E-07 | 6.50E-06 |
| LN-caP | GI50 | 9.34E-07 | 8.50E-08 | 7.11E-07 | - | - | 7.04E-08 | 2.75E-07 | 5.48E-07 | 4.29E-07 | 3.97E-08 | 4.61E-07 |
| | TGI | 1.91E-06 | 3.24E-07 | 4.30E-06 | - | - | 1.69E-07 | 1.27E-06 | 1.45E-06 | 1.67E-06 | 1.55E-07 | 1.57E-06 |
| | LC50 | 3.89E-06 | 1.75E-06 | 1.47E-05 | - | - | 3.96E-07 | 4.90E-06 | 3.43E-06 | 5.08E-06 | 4.23E-07 | 4.11E-06 |
| SKOV-3 | GI50 | 1.67E-06 | 4.96E-08 | 8.74E-07 | - | - | 1.79E-06 | 3.48E-07 | 5.24E-07 | 1.86E-06 | 3.91E-08 | 1.27E-06 |
| | TGI | 3.39E-06 | 3.19E-07 | 5.53E-06 | - | - | 3.90E-06 | 1.24E-06 | 4.22E-06 | 3.67E-06 | 2.28E-07 | 2.91E-06 |
| | LC50 | 6.90E-06 | 7.79E-06 | 1.95E-05 | - | - | 7.35E-06 | 5.36E-06 | 7.62E-06 | 7.27E-06 | 5.03E-06 | 6.65E-06 |
| IGROV | GI50 | 1.23E-06 | 1.08E-07 | 5.04E-07 | 1.15E-06 | 1.64E-06 | 3.67E-07 | 3.50E-07 | 1.26E-06 | 5.61E-07 | 4.96E-08 | 3.07E-07 |
| | TGI | 4.82E-06 | 3.02E-06 | 2.30E-06 | 5.06E-06 | 3.97E-06 | 1.66E-06 | 1.47E-06 | 7.62E-06 | 2.06E-06 | 5.00E-07 | 2.11E-06 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.30E-05 | 1.52E-05 | 9.61E-06 | 7.35E-06 | 6.99E-06 | 7.62E-06 | 6.12E-06 | 4.76E-06 | 8.74E-06 |
| IGROV-ET | GI50 | 1.31E-06 | 1.36E-07 | 5.74E-07 | 1.04E-05 | 1.14E-05 | 5.65E-06 | 4.50E-07 | 1.39E-06 | 6.66E-07 | 7.81E-08 | 2.07E-06 |
| | TGI | 7.13E-06 | 7.79E-07 | 2.08E-06 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 1.83E-06 | 4.00E-06 | 3.01E-06 | 5.89E-07 | 4.63E-06 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 6.63E-06 | 7.62E-06 | 8.76E-06 | 8.83E-06 | 9.10E-06 |
| SK-BR-3 | GI50 | 6.53E-07 | 3.96E-08 | 9.66E-08 | 8.81E-07 | 9.41E-07 | 2.42E-07 | 4.98E-07 | 1.80E-06 | 1.30E-06 | 3.05E-08 | 1.18E-06 |
| | TGI | 1.93E-06 | 1.68E-07 | 1.09E-06 | 3.25E-06 | 4.73E-06 | 5.25E-07 | 1.61E-06 | 7.62E-06 | 3.19E-06 | 1.68E-07 | 3.25E-06 |
| | LC50 | 5.58E-06 | 1.39E-06 | 1.36E-05 | 1.41E-05 | 1.14E-05 | 7.03E-06 | 6.39E-06 | 7.62E-06 | 7.82E-06 | 1.44E-06 | 8.95E-06 |
| MEL-28 | GI50 | 1.38E-06 | 3.92E-08 | 2.08E-06 | 4.47E-06 | 2.24E-06 | 1.55E-06 | 2.51E-07 | 4.82E-07 | 1.35E-06 | 4.11E-08 | 1.36E-06 |
| | TGI | 2.81E-06 | 4.24E-07 | 7.79E-06 | 9.35E-06 | 7.28E-06 | 3.17E-06 | 1.08E-06 | 7.62E-06 | 2.87E-06 | 1.98E-07 | 2.76E-06 |
| | LC50 | 5.74E-06 | 2.95E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 6.45E-06 | 4.42E-06 | 7.62E-06 | 6.13E-06 | 2.48E-06 | 5.58E-06 |
| H-MEC-1 | GI50 | 8.06E-07 | 1.77E-08 | 7.98E-07 | - | - | 2.42E-08 | 7.05E-08 | 1.19E-07 | 2.76E-07 | 9.80E-09 | 2.44E-07 |
| | TGI | 2.20E-06 | 4.13E-08 | 1.95E-05 | - | - | 5.26E-08 | 2.41E-07 | 2.60E-07 | 7.23E-07 | 2.14E-08 | 6.53E-07 |
| | LC50 | 5.97E-06 | 7.79E-06 | 1.95E-05 | - | - | 2.90E-07 | 8.40E-07 | 5.65E-07 | 5.37E-06 | 4.63E-08 | 3.44E-06 |
| A-549 | GI50 | 1.55E-06 | 6.62E-08 | 1.11E-06 | 5.49E-06 | 1.39E-06 | 1.73E-06 | 3.41E-07 | 4.33E-07 | 1.53E-06 | 3.79E-08 | 1.47E-06 |
| | TGI | 3.37E-06 | 1.39E-06 | 8.10E-06 | 1.52E-05 | 1.14E-05 | 3.63E-06 | 1.27E-06 | 1.42E-06 | 3.34E-06 | 1.54E-07 | 3.71E-06 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 6.64E-06 | 4.60E-06 | 7.33E-06 | 8.83E-07 | 9.10E-06 |
| K-562 | GI50 | 6.80E-07 | 5.12E-08 | 7.85E-07 | - | - | 4.81E-07 | 2.04E-07 | 4.10E-07 | 6.73E-07 | 5.96E-09 | 1.04E-06 |
| | TGI | 1.91E-06 | 8.11E-07 | 3.41E-06 | - | - | 3.46E-06 | 1.10E-06 | 2.47E-06 | 2.43E-06 | 9.18E-07 | 2.61E-06 |
| | LC50 | 5.30E-06 | 5.05E-06 | 1.61E-05 | - | - | 7.35E-06 | 8.60E-06 | 7.62E-06 | 8.31E-06 | 4.03E-06 | 6.62E-06 |
| PANC-1 | GI50 | 1.34E-06 | 1.53E-07 | 1.07E-06 | 4.41E-06 | 1.91E-06 | 9.78E-07 | 8.05E-07 | 1.96E-06 | 3.16E-07 | 8.92E-08 | 3.01E-07 |
| | TGI | 6.23E-06 | 3.44E-06 | 8.80E-06 | 1.30E-05 | 1.14E-05 | 4.23E-06 | 2.18E-06 | 7.62E-06 | 1.38E-06 | 1.06E-06 | 9.92E-07 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 5.64E-06 | 7.62E-06 | 8.76E-06 | 8.44E-06 | 9.10E-06 |
| HT-29 | GI50 | 7.13E-06 | 3.17E-06 | 9.17E-06 | 1.44E-07 | 1.11E-07 | 1.84E-06 | 2.81E-06 | 7.62E-06 | 2.66E-06 | 1.34E-06 | 1.16E-06 |
| | TGI | 7.13E-06 | 7.79E-06 | 1.95E-05 | 2.17E-06 | 1.20E-06 | 5.08E-06 | 5.06E-06 | 7.62E-06 | 5.30E-06 | 3.42E-06 | 5.39E-06 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 8.60E-06 | 7.62E-06 | 8.76E-06 | 8.74E-06 | 9.10E-06 |
| LOVO | GI50 | 7.49E-07 | 2.59E-07 | 1.19E-06 | 2.70E-07 | 6.34E-07 | 2.91E-06 | 3.83E-07 | 1.98E-06 | 3.92E-07 | 1.53E-07 | 8.40E-07 |
| | TGI | 1.78E-06 | 1.07E-06 | 1.00E-05 | 2.17E-06 | 5.16E-06 | 7.35E-06 | 1.06E-06 | 5.35E-06 | 1.65E-06 | 3.33E-07 | 4.02E-06 |
| | LC50 | 4.28E-06 | 5.41E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 3.77E-06 | 7.62E-06 | 6.31E-06 | 7.26E-07 | 9.10E-06 |
| LOVO-DOX | GI50 | 8.91E-07 | 2.44E-07 | 8.67E-07 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 6.83E-07 | 1.49E-06 | 6.71E-07 | 1.98E-07 | 9.10E-06 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 3.66E-06 | 1.32E-06 | 7.63E-06 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 1.93E-06 | 7.62E-06 | 2.42E-06 | 5.58E-07 | 9.10E-06 |
| | LC50 | 7.13E-06 | 7.79E-06 | 1.95E-05 | 1.52E-05 | 1.14E-05 | 7.35E-06 | 5.22E-06 | 7.62E-06 | 8.25E-06 | 4.33E-06 | 9.10E-06 |
| HELA | GI50 | - | - | - | 4.04E-06 | 2.76E-06 | - | - | - | - | - | - |
| | TGI | - | - | - | 9.47E-06 | 9.24E-06 | - | - | - | - | - | - |
| | LC50 | - | - | - | 1.52E-05 | 1.14E-05 | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | 1.30E-05 | 9.53E-06 | - | - | - | - | - | - |
| | TGI | - | - | - | 1.52E-05 | 1.14E-05 | - | - | - | - | - | - |
| | LC50 | - | - | - | 1.52E-05 | 1.14E-05 | - | - | - | - | - | - |

| | | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 3.21E-08 | 1.08E-08 | 6.77E-08 | 5.12E-08 | 1.80E-08 | 1.62E-08 | 6.79E-07 | 3.65E-07 | 5.74E-08 | 4.85E-08 | 1.05E-07 | 3.80E-07 |
| | TGI | 8.81E-08 | 3.83E-08 | 1.55E-06 | 9.11E-06 | 1.42E-07 | 9.40E-08 | 9.87E-06 | 2.28E-06 | 3.01E-07 | 2.73E-07 | 5.49E-07 | 2.19E-06 |
| | LC50 | 5.76E-07 | 6.68E-07 | 5.62E-06 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 8.54E-06 |
| LN-caP | GI50 | 8.81E-08 | 4.28E-08 | 5.93E-07 | 1.52E-07 | 2.79E-08 | 1.30E-07 | 2.10E-06 | 3.77E-07 | - | - | - | 2.09E-06 |
| | TGI | 4.68E-07 | 1.56E-07 | 2.18E-06 | 5.09E-07 | 2.52E-07 | 4.47E-07 | 6.47E-06 | 1.41E-06 | - | - | - | 6.58E-06 |
| | LC50 | 2.22E-06 | 4.24E-07 | 5.05E-06 | 3.90E-06 | 8.47E-06 | 4.38E-06 | 9.87E-06 | 4.91E-06 | - | - | - | 9.57E-06 |
| SKOV-3 | GI50 | 1.13E-07 | 3.92E-08 | 1.62E-06 | 6.84E-07 | 6.34E-08 | 2.84E-08 | 5.95E-06 | 1.24E-06 | 1.46E-07 | 9.88E-08 | 1.75E-07 | 3.16E-06 |
| | TGI | 9.32E-07 | 2.97E-07 | 3.58E-06 | 7.42E-06 | 8.47E-06 | 1.07E-07 | 9.87E-06 | 4.44E-06 | 1.14E-06 | 1.15E-06 | 2.20E-06 | 9.57E-06 |
| | LC50 | 3.83E-06 | 5.89E-06 | 7.87E-06 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| IGROV | GI50 | 1.52E-07 | 4.69E-08 | 5.77E-07 | 2.44E-07 | 3.41E-08 | 4.49E-08 | 9.17E-08 | 1.85E-07 | 4.18E-07 | 1.06E-06 | 1.57E-06 | 2.77E-07 |
| | TGI | 9.07E-07 | 4.09E-07 | 2.17E-06 | 1.07E-06 | 9.31E-07 | 3.91E-07 | 4.92E-07 | 5.60E-07 | 2.14E-06 | 2.32E-06 | 4.12E-06 | 2.15E-06 |
| | LC50 | 4.05E-06 | 7.95E-06 | 5.89E-06 | 9.11E-06 | 8.47E-06 | 5.04E-06 | 4.70E-06 | 2.83E-06 | 8.94E-06 | 5.06E-06 | 1.09E-05 | 9.57E-06 |
| IGROV-ET | GI50 | 1.92E-07 | 7.65E-08 | 3.59E-07 | 1.29E-06 | 5.50E-08 | 8.52E-08 | 1.88E-07 | 2.38E-07 | 9.80E-08 | 1.18E-06 | 2.58E-06 | 4.99E-07 |
| | TGI | 8.55E-07 | 5.40E-07 | 2.11E-06 | 4.51E-06 | 3.69E-07 | 5.57E-07 | 8.52E-07 | 6.78E-07 | 3.24E-06 | 3.58E-06 | 8.07E-06 | 3.03E-06 |
| | LC50 | 5.45E-06 | 8.78E-06 | 8.04E-06 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 6.62E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| SK-BR-3 | GI50 | 2.28E-07 | 3.96E-08 | 5.76E-08 | 4.48E-07 | 5.45E-08 | 8.16E-07 | 1.62E-06 | 2.00E-06 | 2.12E-07 | 1.22E-07 | 4.14E-07 | 1.93E-06 |
| | TGI | 6.89E-07 | 2.21E-07 | 2.12E-06 | 4.08E-06 | 1.46E-06 | 3.25E-06 | 4.85E-06 | 4.01E-06 | 1.10E-06 | 8.66E-07 | 1.58E-06 | 4.67E-06 |
| | LC50 | 4.03E-06 | 2.94E-06 | 1.06E-05 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 8.04E-06 | 7.90E-06 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| MEL-28 | GI50 | 5.46E-08 | 3.19E-08 | 6.23E-07 | 1.65E-07 | 3.39E-08 | 4.12E-08 | 1.86E-06 | 1.23E-06 | 4.98E-07 | 4.80E-07 | 8.98E-07 | 1.22E-06 |
| | TGI | 9.15E-07 | 1.81E-07 | 2.68E-06 | 5.20E-07 | 2.95E-07 | 5.95E-07 | 4.19E-06 | 3.32E-06 | 1.21E-05 | 3.21E-06 | 1.15E-05 | 9.57E-06 |
| | LC50 | 2.77E-06 | 2.70E-06 | 7.95E-06 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.43E-06 | 8.94E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| H-MEC-1 | GI50 | 1.97E-08 | 2.65E-09 | 9.74E-08 | 8.09E-08 | 6.98E-09 | - | - | - | - | - | - | 1.95E-07 |
| | TGI | 4.03E-08 | 8.60E-09 | 1.26E-06 | 9.11E-07 | 8.47E-06 | - | - | - | - | - | - | 9.57E-06 |
| | LC50 | 8.26E-08 | 1.35E-06 | 4.73E-06 | 9.11E-06 | 8.47E-06 | - | - | - | - | - | - | 9.57E-06 |
| A-549 | GI50 | 5.24E-08 | 3.28E-08 | 1.72E-06 | 1.34E-06 | 4.64E-08 | 3.16E-08 | 2.42E-06 | 7.35E-07 | 1.90E-06 | 5.44E-06 | 4.35E-06 | 1.31E-06 |
| | TGI | 2.59E-07 | 1.54E-07 | 3.80E-06 | 4.78E-06 | 8.55E-07 | 2.70E-07 | 8.01E-06 | 2.99E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| | LC50 | 6.09E-06 | 1.69E-06 | 8.38E-06 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| K-562 | GI50 | 8.08E-08 | 9.48E-09 | 1.24E-08 | 4.13E-08 | 3.59E-08 | 5.82E-08 | 1.77E-06 | 3.13E-07 | 1.18E-07 | 1.82E-07 | 3.15E-07 | 2.25E-06 |
| | TGI | 9.75E-07 | 1.88E-07 | 1.97E-06 | 1.15E-06 | 1.08E-06 | 9.86E-07 | 3.76E-06 | 1.79E-06 | 5.65E-07 | 6.86E-07 | 1.73E-06 | 6.53E-06 |
| | LC50 | 4.82E-06 | 5.70E-06 | 7.53E-06 | 9.11E-06 | 8.47E-06 | 4.61E-06 | 8.02E-06 | 5.42E-06 | 1.21E-05 | 5.36E-06 | 8.79E-06 | 9.57E-06 |
| PANC-1 | GI50 | 1.78E-07 | 1.69E-07 | 2.15E-06 | 4.99E-07 | 1.64E-07 | 2.54E-07 | 2.48E-06 | 7.32E-07 | 1.49E-06 | 1.17E-06 | 2.03E-06 | 1.34E-06 |
| | TGI | 1.21E-06 | 1.13E-06 | 1.10E-05 | 9.11E-06 | 8.47E-06 | 3.27E-06 | 9.87E-06 | 4.06E-06 | 6.57E-06 | 4.35E-06 | 9.75E-06 | 9.57E-06 |
| | LC50 | 3.67E-06 | 8.78E-06 | 1.10E-05 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| HT-29 | GI50 | 1.18E-06 | 1.51E-06 | 9.12E-08 | 3.24E-08 | 3.04E-06 | 3.57E-06 | 3.24E-06 | 3.91E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 2.28E-06 |
| | TGI | 2.44E-06 | 4.08E-06 | 2.00E-06 | 9.11E-08 | 8.47E-06 | 9.48E-06 | 8.89E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| | LC50 | 5.06E-06 | 8.78E-06 | 1.09E-05 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| LOVO | GI50 | 2.07E-07 | 1.58E-07 | 1.79E-06 | 9.11E-06 | 3.21E-07 | 2.23E-07 | 3.31E-06 | 4.63E-07 | 6.35E-07 | 3.74E-07 | 7.71E-07 | 4.23E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 7.05E-07 | 3.21E-07 | 4.40E-06 | 9.11E-06 | 2.53E-06 | 8.84E-07 | 9.87E-06 | 3.63E-06 | 3.72E-06 | 3.18E-06 | 6.71E-06 | 9.57E-06 |
| | LC50 | 2.60E-06 | 6.52E-07 | 1.08E-05 | 9.11E-06 | 8.47E-06 | 6.41E-06 | 9.87E-06 | 9.46E-06 | 1.21E-05 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| LOVO-DOX | GI50 | 2.17E-07 | 1.45E-07 | 2.10E-06 | 9.11E-06 | 3.23E-07 | 4.70E-07 | 4.20E-06 | 3.95E-07 | 9.37E-07 | 6.08E-07 | 7.78E-07 | 6.57E-06 |
| | TGI | 7.37E-07 | 5.25E-07 | 4.60E-06 | 9.11E-06 | 1.81E-06 | 3.35E-06 | 9.87E-06 | 2.32E-06 | 3.14E-06 | 2.51E-06 | 4.51E-06 | 9.57E-06 |
| | LC50 | 2.80E-06 | 8.78E-06 | 1.01E-05 | 9.11E-06 | 8.47E-06 | 9.48E-06 | 9.87E-06 | 9.46E-06 | 9.84E-06 | 7.60E-06 | 1.15E-05 | 9.57E-06 |
| HELA | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |

Table II

| | | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | 57 | 58 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.08E-06 | 1.10E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.33E-06 | 4.53E-06 | 2.88E-06 | 1.14E-05 | 3.33E-06 | 3.89E-06 | 9.92E-06 |
| | TGI | 4.61E-06 | 3.56E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 4.08E-06 | 1.23E-05 | 7.16E-06 | 1.14E-05 | 1.19E-05 | 1.22E-05 | 9.92E-06 |
| | LC50 | 1.03E-05 | 8.80E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| LN-caP | GI50 | 8.84E-08 | 2.13E-06 | 1.52E-05 | 1.60E-05 | 7.26E-06 | 1.85E-06 | 4.01E-06 | 1.71E-06 | - | 1.32E-06 | 2.16E-06 | 8.07E-06 |
| | TGI | 1.59E-06 | 4.90E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 4.54E-06 | 9.75E-06 | 4.34E-06 | - | 5.24E-06 | 5.47E-06 | 9.92E-06 |
| | LC50 | 5.87E-06 | 1.13E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.11E-05 | - | 1.19E-05 | 1.39E-05 | 9.92E-06 |
| SKOV-3 | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| IGROV | GI50 | 7.64E-07 | 1.20E-06 | 1.52E-05 | 1.60E-05 | 9.94E-06 | 1.02E-06 | 1.38E-06 | 8.84E-07 | 1.11E-05 | 1.64E-06 | 8.47E-07 | 9.92E-06 |
| | TGI | 1.03E-05 | 5.16E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 3.32E-06 | 2.01E-05 | 4.02E-06 | 1.14E-05 | 7.92E-06 | 5.88E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.88E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.04E-05 | 2.01E-05 | 1.33E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| IGROV-ET | GI50 | 2.07E-06 | 1.21E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 2.26E-06 | 2.01E-05 | 6.64E-06 | 1.14E-05 | 1.19E-05 | 8.90E-07 | 9.92E-06 |
| | TGI | 1.03E-05 | 4.58E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 6.96E-06 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 6.43E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.76E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| SK-BR-3 | GI50 | 2.29E-06 | 1.71E-06 | 1.52E-05 | 1.60E-05 | 7.13E-06 | 1.11E-06 | 1.99E-06 | 1.05E-06 | 4.58E-06 | 1.60E-06 | 3.17E-07 | 4.04E-06 |
| | TGI | 6.01E-06 | 4.39E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 3.50E-06 | 9.49E-06 | 4.31E-06 | 1.14E-05 | 4.05E-06 | 5.24E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.10E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.02E-05 | 1.95E-05 | 9.92E-06 |
| MEL-28 | GI50 | 2.07E-06 | 4.00E-06 | - | 1.60E-05 | 4.81E-06 | 1.25E-06 | 4.03E-06 | 1.53E-06 | 1.14E-05 | 3.35E-06 | 1.68E-06 | 9.92E-06 |
| | TGI | 1.03E-05 | 7.09E-06 | - | 1.60E-05 | 1.10E-05 | 6.63E-06 | 1.55E-05 | 5.70E-06 | 1.14E-05 | 1.06E-05 | 1.26E-05 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.26E-05 | - | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| H-MEC-1 | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| A-549 | GI50 | 3.26E-06 | 2.85E-06 | 1.52E-05 | 1.60E-05 | 9.76E-06 | 2.86E-06 | 5.66E-06 | 2.85E-06 | 1.14E-05 | 3.47E-06 | 1.29E-06 | 9.92E-06 |
| | TGI | 1.03E-05 | 6.60E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.51E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.53E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| K-562 | GI50 | 5.64E-07 | 2.68E-06 | 1.52E-05 | 1.44E-05 | 1.10E-05 | 3.15E-06 | 1.03E-05 | 3.76E-06 | - | 3.19E-06 | 2.69E-06 | 9.92E-06 |
| | TGI | 3.74E-06 | 6.07E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.42E-05 | - | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.37E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | - | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| PANC-1 | GI50 | 3.86E-06 | 2.26E-06 | 1.52E-05 | 1.60E-05 | 8.48E-06 | 1.70E-06 | 1.03E-06 | 7.11E-07 | 1.14E-05 | 3.41E-06 | 6.11E-07 | 9.92E-06 |
| | TGI | 1.03E-05 | 5.05E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 7.40E-06 | 9.67E-06 | 2.59E-06 | 1.14E-05 | 7.83E-06 | 9.70E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.13E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| HT-29 | GI50 | 1.25E-06 | 6.97E-06 | 1.52E-05 | 1.60E-05 | 9.93E-06 | 2.36E-06 | 2.17E-06 | 1.52E-06 | 1.10E-05 | 4.04E-06 | 3.49E-06 | 9.92E-06 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 1.03E-05 | 1.16E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.88E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| LOVO | GI50 | 3.97E-06 | 3.64E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.56E-06 | 1.11E-05 | 3.40E-06 | 7.21E-06 | 5.21E-06 | 7.17E-07 | 9.92E-06 |
| | TGI | 1.03E-05 | 6.80E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 4.91E-06 | 2.01E-05 | 8.94E-06 | 1.14E-05 | 1.19E-05 | 5.30E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.27E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| LOVO-DOX | GI50 | 8.09E-06 | 4.03E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 4.34E-06 | 2.01E-05 | 1.25E-05 | 1.14E-05 | 1.19E-05 | 8.28E-07 | 9.92E-06 |
| | TGI | 1.03E-05 | 7.63E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 6.91E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.44E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| HELA | GI50 | 5.37E-07 | 3.54E-06 | 1.52E-05 | 1.60E-05 | 7.95E-06 | 1.36E-06 | 5.90E-07 | 6.16E-07 | 3.75E-06 | 1.69E-06 | 6.85E-07 | 9.92E-06 |
| | TGI | 4.79E-06 | 6.88E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 5.88E-06 | 1.23E-05 | 2.71E-06 | 1.14E-05 | 5.83E-06 | 5.67E-06 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.34E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |
| HELA-APL | GI50 | 5.75E-06 | 2.66E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 2.81E-06 | 2.01E-05 | 3.83E-06 | 4.58E-06 | 1.19E-05 | 3.68E-06 | 9.92E-06 |
| | TGI | 1.03E-05 | 5.18E-06 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.10E-05 | 9.92E-06 |
| | LC50 | 1.03E-05 | 1.01E-05 | 1.52E-05 | 1.60E-05 | 1.10E-05 | 1.10E-05 | 2.01E-05 | 1.72E-05 | 1.14E-05 | 1.19E-05 | 1.95E-05 | 9.92E-06 |

| | | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 | 67 | 68 | 69 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.39E-06 | 1.18E-06 | 3.77E-06 | 4.69E-06 | 2.20E-06 | 4.89E-06 | 1.09E-05 | 1.73E-06 | 2.72E-06 | 2.95E-06 | 1.67E-05 |
| | TGI | 2.60E-06 | 2.65E-06 | 8.22E-06 | 9.82E-06 | 5.08E-06 | 1.36E-05 | 1.09E-05 | 3.65E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 4.86E-06 | 5.97E-06 | 1.60E-05 | 9.82E-06 | 1.17E-05 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| LN-caP | GI50 | 1.37E-06 | 5.50E-07 | 3.24E-06 | 1.63E-06 | 1.13E-06 | 1.94E-06 | 3.12E-06 | 8.90E-07 | 1.30E-06 | 3.78E-06 | 1.54E-05 |
| | TGI | 2.63E-06 | 1.79E-06 | 6.04E-06 | 3.11E-06 | 3.47E-06 | 7.21E-06 | 8.87E-06 | 1.89E-06 | 2.53E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 5.06E-06 | 5.25E-06 | 1.13E-05 | 5.93E-06 | 9.61E-06 | 1.36E-05 | 1.09E-05 | 4.03E-06 | 4.93E-06 | 7.33E-06 | 1.67E-05 |
| SKOV-3 | GI50 | - | - | - | - | 3.06E-06 | 5.96E-06 | 1.09E-05 | 2.85E-06 | 6.00E-06 | 3.15E-06 | - |
| | TGI | - | - | - | - | 5.84E-06 | 1.36E-05 | 1.09E-05 | 6.28E-06 | 6.00E-06 | 7.33E-06 | - |
| | LC50 | - | - | - | - | 1.11E-05 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | - |
| IGROV | GI50 | 8.99E-07 | 6.82E-07 | 3.85E-06 | 2.90E-06 | 9.75E-07 | 3.57E-06 | 9.89E-06 | 1.35E-06 | 2.53E-06 | 3.88E-06 | 1.67E-05 |
| | TGI | 2.63E-06 | 3.29E-06 | 8.81E-06 | 9.03E-06 | 3.86E-06 | 1.11E-05 | 1.09E-05 | 3.02E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 7.67E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 1.46E-05 | 1.36E-05 | 1.09E-05 | 6.75E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| IGROV-ET | GI50 | 6.32E-07 | 2.56E-06 | 7.62E-06 | 9.82E-06 | 6.40E-07 | 7.75E-06 | 1.09E-05 | 1.22E-06 | 6.00E-06 | 7.33E-06 | 9.35E-06 |
| | TGI | 2.04E-06 | 6.16E-06 | 1.60E-05 | 9.82E-06 | 2.86E-06 | 1.36E-05 | 1.09E-05 | 2.90E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 5.98E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 1.52E-05 | 1.36E-05 | 1.09E-05 | 6.87E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| SK-BR-3 | GI50 | 3.72E-07 | 4.91E-07 | 3.26E-06 | 1.17E-06 | 1.57E-06 | 1.76E-06 | 1.16E-06 | 4.34E-07 | 1.97E-06 | 3.23E-06 | 1.67E-05 |
| | TGI | 1.15E-06 | 1.64E-06 | 6.91E-06 | 3.23E-06 | 4.80E-06 | 7.10E-06 | 5.54E-06 | 1.82E-06 | 5.59E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 4.11E-06 | 8.58E-06 | 1.46E-05 | 8.99E-06 | 1.47E-05 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| MEL-28 | GI50 | 1.62E-06 | 1.17E-06 | 3.80E-06 | 2.55E-06 | 2.34E-06 | 3.57E-06 | 1.09E-05 | 1.42E-06 | 1.56E-06 | 3.73E-06 | 1.67E-05 |
| | TGI | 3.04E-06 | 4.14E-06 | 1.13E-05 | 5.28E-06 | 4.87E-06 | 1.36E-05 | 1.09E-05 | 2.55E-06 | 3.71E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 5.67E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 1.01E-05 | 1.36E-05 | 1.09E-05 | 4.55E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| H-MEC-1 | GI50 | - | - | - | - | 2.72E-06 | 3.22E-06 | 2.33E-06 | 1.52E-06 | 1.89E-06 | 2.38E-06 | - |
| | TGI | - | - | - | - | 5.25E-06 | 7.99E-06 | 4.42E-06 | 2.73E-06 | 3.46E-06 | 5.42E-06 | - |
| | LC50 | - | - | - | - | 1.01E-05 | 1.36E-05 | 8.38E-06 | 4.93E-06 | 6.00E-06 | 7.33E-06 | - |
| A-549 | GI50 | 1.70E-06 | 1.62E-06 | 3.21E-06 | 3.60E-06 | 2.84E-06 | 6.46E-06 | 1.09E-05 | 1.86E-06 | 6.00E-06 | 4.13E-06 | 1.67E-05 |
| | TGI | 3.29E-06 | 4.63E-06 | 9.54E-06 | 9.82E-06 | 5.57E-06 | 1.36E-05 | 1.09E-05 | 3.46E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 6.36E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 1.09E-05 | 1.36E-05 | 1.09E-05 | 6.43E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| K-562 | GI50 | 1.64E-06 | 6.97E-07 | 5.59E-06 | 2.63E-06 | 2.90E-06 | 1.36E-05 | 2.37E-06 | 9.82E-07 | 2.02E-06 | 7.33E-06 | 6.41E-06 |
| | TGI | 3.45E-06 | 2.19E-06 | 1.13E-05 | 4.39E-06 | 6.75E-06 | 1.36E-05 | 6.64E-06 | 2.80E-06 | 6.00E-06 | 7.33E-06 | 8.54E-06 |
| | LC50 | 7.27E-06 | 6.87E-06 | 1.60E-05 | 7.33E-06 | 1.52E-05 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.13E-05 |
| PANC-1 | GI50 | 1.10E-06 | 7.47E-07 | 5.98E-06 | 5.31E-06 | 1.93E-06 | 4.20E-06 | 5.74E-06 | 1.95E-06 | 2.57E-06 | 4.21E-06 | 1.67E-05 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 3.48E-06 | 4.40E-06 | 1.50E-05 | 9.82E-06 | 5.05E-06 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 8.81E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 1.32E-05 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| HT-29 | GI50 | 1.97E-06 | 2.42E-06 | 6.27E-06 | 1.05E-06 | 2.92E-06 | 3.31E-06 | 5.03E-06 | 2.77E-06 | 2.51E-06 | 3.95E-06 | 1.67E-05 |
| | TGI | 3.70E-06 | 5.88E-06 | 1.58E-05 | 9.82E-06 | 5.70E-06 | 1.36E-05 | 1.09E-05 | 6.77E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 6.98E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 1.11E-05 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| LOVO | GI50 | 1.13E-06 | 1.61E-06 | 4.44E-06 | 9.82E-06 | 1.46E-06 | 5.08E-06 | 1.09E-05 | 2.19E-06 | 6.00E-06 | 4.26E-06 | 1.67E-05 |
| | TGI | 2.53E-06 | 3.58E-06 | 1.08E-05 | 9.82E-06 | 3.68E-06 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 5.67E-06 | 7.94E-06 | 1.60E-05 | 9.82E-06 | 9.11E-06 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| LOVO-DOX | GI50 | 5.28E-07 | 2.82E-06 | 1.33E-05 | 9.82E-06 | 9.09E-07 | 1.36E-05 | 1.09E-05 | 1.91E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | TGI | 1.60E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 2.95E-06 | 1.36E-05 | 1.09E-05 | 5.56E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| | LC50 | 4.56E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | 9.85E-06 | 1.36E-05 | 1.09E-05 | 7.12E-06 | 6.00E-06 | 7.33E-06 | 1.67E-05 |
| HELA | GI50 | 1.37E-06 | 1.02E-06 | 3.66E-06 | 2.03E-06 | - | - | - | - | - | - | 1.67E-05 |
| | TGI | 2.98E-06 | 2.51E-06 | 9.67E-06 | 4.09E-06 | - | - | - | - | - | - | 1.67E-05 |
| | LC50 | 6.44E-06 | 6.13E-06 | 1.60E-05 | 8.22E-06 | - | - | - | - | - | - | 1.67E-05 |
| HELA-APL | GI50 | 1.88E-06 | 3.49E-06 | 7.88E-06 | 2.76E-06 | - | - | - | - | - | - | 1.67E-05 |
| | TGI | 3.90E-06 | 9.15E-06 | 1.60E-05 | 8.14E-06 | - | - | - | - | - | - | 1.67E-05 |
| | LC50 | 8.12E-06 | 9.15E-06 | 1.60E-05 | 9.82E-06 | - | - | - | - | - | - | 1.67E-05 |

| | | 70 | 71 | 72 | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 | 81 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 9.27E-06 | 7.58E-06 | 5.30E-06 | 1.08E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.48E-06 | 4.05E-06 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | TGI | 1.94E-05 | 7.58E-06 | 1.21E-05 | 8.81E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 5.47E-06 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| LN-caP | GI50 | - | - | - | - | - | - | - | 1.31E-06 | 5.61E-06 | 3.60E-06 | 4.20E-06 | 1.11E-05 |
| | TGI | - | - | - | - | - | - | - | 3.68E-06 | 1.10E-05 | 9.87E-06 | 9.46E-06 | 1.11E-05 |
| | LC50 | - | - | - | - | - | - | - | 1.04E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| SKOV-3 | GI50 | 6.92E-06 | 2.62E-06 | 3.94E-06 | 4.54E-06 | 3.14E-06 | 8.86E-06 | 8.54E-06 | - | 9.70E-06 | 8.69E-06 | 7.60E-06 | 1.11E-05 |
| | TGI | 1.68E-05 | 6.37E-06 | 7.78E-06 | 8.81E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | - | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | - | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| IGROV | GI50 | 4.92E-06 | 1.58E-06 | 1.53E-06 | 2.99E-06 | 3.21E-06 | 5.22E-06 | 4.86E-06 | 7.78E-07 | 5.78E-06 | 4.27E-06 | 3.28E-06 | 1.11E-05 |
| | TGI | 8.90E-06 | 3.34E-06 | 3.51E-06 | 5.40E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.04E-05 | 1.10E-05 | 9.09E-06 | 6.41E-06 | 1.11E-05 |
| | LC50 | 1.61E-05 | 7.06E-06 | 8.07E-06 | 9.78E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| IGROV-ET | GI50 | 9.02E-06 | 2.78E-06 | 1.91E-06 | 5.01E-06 | 5.37E-06 | 8.86E-06 | 8.54E-06 | 4.63E-06 | 1.10E-05 | 1.11E-05 | 1.14E-05 | 1.11E-05 |
| | TGI | 1.94E-05 | 7.28E-06 | 4.34E-06 | 7.45E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 9.92E-06 | 1.11E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| SK-BR-3 | GI50 | 2.76E-06 | 1.94E-06 | 1.34E-06 | 1.99E-06 | 2.04E-06 | 4.04E-06 | 3.10E-06 | 2.59E-07 | 1.10E-05 | 4.78E-06 | 3.32E-06 | 1.11E-05 |
| | TGI | 7.05E-06 | 3.95E-06 | 3.79E-06 | 4.29E-06 | 3.74E-06 | 8.86E-06 | 8.25E-06 | 9.77E-07 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.80E-05 | 7.58E-06 | 1.07E-05 | 9.29E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 7.31E-06 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| MEL-28 | GI50 | 6.92E-06 | 1.66E-06 | 2.42E-06 | 2.34E-06 | 3.61E-06 | 8.86E-06 | 8.54E-06 | 8.58E-07 | 1.10E-05 | 1.11E-05 | 8.33E-06 | 1.11E-05 |
| | TGI | 1.54E-05 | 3.25E-06 | 4.21E-06 | 4.06E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 6.38E-06 | 7.32E-06 | 7.06E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| H-MEC-1 | GI50 | 2.90E-06 | 2.66E-06 | 3.47E-06 | 9.12E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | - | 1.10E-05 | 1.11E-05 | 1.18E-05 | 4.98E-06 |
| | TGI | 9.74E-06 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | - | 1.10E-05 | 1.11E-05 | 1.18E-05 | 7.66E-06 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | - | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| A-549 | GI50 | 1.94E-05 | 5.89E-06 | 8.02E-06 | 1.15E-05 | 5.94E-06 | 8.86E-06 | 8.54E-06 | 2.61E-07 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | TGI | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 3.51E-06 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| K-562 | GI50 | 5.11E-06 | 1.08E-06 | 1.93E-06 | 2.42E-06 | 1.21E-06 | 5.49E-06 | 4.18E-06 | 6.92E-06 | 8.12E-06 | 8.90E-06 | 5.04E-06 | 1.11E-05 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 1.12E-06 | 2.12E-06 | 3.68E-06 | 4.28E-06 | 2.43E-06 | 8.86E-06 | 8.54E-06 | 3.51E-06 | 1.10E-06 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 4.15E-06 | 7.01E-06 | 7.59E-06 | 4.87E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-06 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| PANC-1 | GI50 | 5.69E-06 | 2.37E-06 | 2.40E-06 | 2.74E-06 | 4.44E-06 | 5.49E-06 | 8.54E-06 | 2.58E-06 | 1.10E-05 | 1.11E-05 | 1.00E-05 | 1.11E-05 |
| | TGI | 1.46E-05 | 5.99E-06 | 5.45E-06 | 5.74E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| HT-29 | GI50 | 1.94E-05 | 7.58E-06 | 9.17E-06 | 7.83E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 2.61E-07 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | TGI | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 2.70E-06 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.21E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| LOVO | GI50 | 4.96E-06 | 3.78E-06 | 2.30E-06 | 2.81E-06 | 4.14E-06 | 8.86E-06 | 8.54E-06 | 4.79E-06 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | TGI | 1.44E-05 | 7.58E-06 | 5.08E-06 | 5.80E-06 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 7.58E-06 | 1.12E-05 | 1.15E-05 | 6.18E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| LOVO-DOX | GI50 | 6.88E-06 | 1.50E-06 | 2.07E-06 | 2.26E-06 | 1.17E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 9.05E-06 | 1.11E-05 |
| | TGI | 1.33E-05 | 2.81E-06 | 4.03E-06 | 4.33E-06 | 2.27E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| | LC50 | 1.94E-05 | 5.23E-06 | 7.84E-06 | 8.32E-06 | 4.39E-06 | 8.86E-06 | 8.54E-06 | 1.17E-05 | 1.10E-05 | 1.11E-05 | 1.18E-05 | 1.11E-05 |
| HELA | GI50 | - | - | - | - | - | - | - | 1.46E-06 | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | 7.26E-06 | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | 1.17E-05 | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | 9.59E-06 | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | 1.17E-05 | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | 1.17E-05 | - | - | - | - |

| | | 82 | 83 | 84 | 85 | 86 | 87 | 88 | 89 | 90 | 91 | 92 | 93 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.15E-05 | 9.19E-06 | 3.41E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | TGI | 1.15E-05 | 9.19E-06 | 8.36E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| LN-caP | GI50 | 1.66E-07 | 9.19E-06 | 7.10E-07 | 5.14E-06 | 5.31E-06 | 1.07E-05 | 2.59E-08 | 1.44E-08 | 1.14E-05 | 7.52E-06 | 1.67E-07 | 4.08E-07 |
| | TGI | 1.15E-05 | 9.19E-06 | 2.01E-06 | 1.21E-05 | 9.52E-06 | 1.07E-05 | 8.79E-08 | 7.36E-08 | 1.14E-05 | 1.23E-05 | 7.10E-07 | 1.27E-06 |
| | LC50 | 1.15E-05 | 9.19E-06 | 5.21E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-06 | 3.96E-04 | 1.14E-05 | 1.66E-05 | 5.09E-06 | 7.08E-06 |
| SKOV-3 | GI50 | 1.15E-05 | 9.19E-06 | 4.58E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 6.43E-06 | 9.82E-06 | 1.14E-05 | 1.04E-05 | 7.61E-06 | 6.26E-06 |
| | TGI | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| IGROV | GI50 | 1.15E-05 | 9.19E-06 | 2.41E-06 | 5.45E-06 | 4.03E-06 | 4.58E-06 | 3.79E-06 | 3.10E-06 | 1.10E-05 | 5.30E-06 | 3.13E-06 | 3.37E-06 |
| | TGI | 1.15E-05 | 9.19E-06 | 6.28E-06 | 1.40E-05 | 9.30E-06 | 1.07E-05 | 6.82E-06 | 6.01E-06 | 1.14E-05 | 9.06E-06 | 6.64E-06 | 7.08E-06 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.55E-05 | 1.41E-05 | 1.28E-05 |
| IGROV-ET | GI50 | 6.67E-06 | 9.19E-06 | 4.26E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.04E-05 | 6.85E-06 | 1.17E-05 |
| | TGI | 1.15E-05 | 9.19E-06 | 8.25E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| SK-BR-3 | GI50 | 1.15E-05 | 9.19E-06 | 4.60E-07 | 1.30E-05 | 1.11E-05 | 1.07E-05 | 5.01E-06 | 5.08E-06 | 1.14E-05 | 5.40E-06 | 4.35E-06 | 4.95E-06 |
| | TGI | 1.15E-05 | 9.19E-06 | 9.50E-07 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.05E-05 | 1.16E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| MEL-28 | GI50 | 1.15E-05 | 9.19E-06 | 2.07E-06 | 1.48E-05 | 9.72E-06 | 1.07E-05 | 4.90E-06 | 7.92E-06 | 1.14E-05 | 5.28E-06 | 4.75E-06 | 4.57E-06 |
| | TGI | 1.15E-05 | 9.19E-06 | 3.86E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.07E-05 | 1.01E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 7.21E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| H-MEC-1 | GI50 | 6.13E-06 | 9.19E-06 | 6.82E-07 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.25E-05 | 1.42E-05 | 1.28E-05 |
| | TGI | 8.16E-06 | 9.19E-06 | 1.86E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.09E-05 | 9.19E-06 | 5.96E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| A-549 | GI50 | 1.15E-05 | 9.19E-06 | 2.66E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 8.64E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 1.15E-05 | 9.19E-06 | 4.91E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.03E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| K-562 | GI50 | 1.15E-05 | 9.12E-06 | 7.31E-07 | 3.18E-06 | 8.30E-06 | 5.10E-06 | 4.41E-04 | 9.82E-06 | 1.14E-05 | 2.67E-06 | 2.23E-06 | 1.62E-06 |
| | TGI | 1.15E-05 | 9.19E-06 | 3.30E-06 | 5.74E-06 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 4.42E-06 | 1.38E-05 | 2.65E-06 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.04E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 7.32E-06 | 1.49E-05 | 4.36E-06 |
| PANC-1 | GI50 | 1.15E-05 | 9.19E-06 | 5.01E-07 | 1.20E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 8.53E-06 | 5.42E-06 | 1.28E-05 |
| | TGI | 1.15E-05 | 9.19E-06 | 5.47E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| HT-29 | GI50 | 1.15E-05 | 9.19E-06 | 2.34E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.63E-05 | 1.49E-05 | 1.28E-05 |
| | TGI | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| LOVO | GI50 | 1.15E-05 | 9.19E-06 | 4.48E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 7.49E-06 | 9.82E-06 | 1.14E-05 | 6.20E-06 | 7.52E-06 | 1.28E-05 |
| | TGI | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.20E-05 | 1.49E-05 | 1.28E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| LOVO-DOX | GI50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 6.40E-06 | 1.07E-05 | 3.63E-06 | 9.82E-06 | 1.14E-05 | 5.78E-06 | 2.14E-06 | 3.39E-06 |
| | TGI | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 7.04E-06 | 9.82E-06 | 1.14E-05 | 1.12E-05 | 5.96E-06 | 1.17E-05 |
| | LC50 | 1.15E-05 | 9.19E-06 | 9.90E-06 | 1.48E-05 | 1.28E-05 | 1.07E-05 | 1.09E-05 | 9.82E-06 | 1.14E-05 | 1.66E-05 | 1.49E-05 | 1.28E-05 |
| HELA | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |

| | | 94 | 95 | 96 | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 | 105 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.31E-05 | 1.94E-05 | 4.26E-06 | 4.13E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| LN-caP | GI50 | 6.73E-07 | 3.63E-06 | - | - | 1.98E-06 | 4.46E-06 | 1.06E-05 | 8.25E-06 | 1.09E-05 | 3.94E-06 | 1.52E-05 | 3.62E-06 |
| | TGI | 2.87E-06 | 6.09E-06 | - | - | 6.22E-06 | 8.19E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.49E-05 | 1.52E-05 | 7.91E-06 |
| | LC50 | 1.25E-05 | 1.02E-05 | - | - | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| SKOV-3 | GI50 | 8.48E-06 | 1.39E-05 | 4.20E-06 | 6.01E-06 | 7.06E-06 | 9.44E-06 | 1.08E-05 | 7.91E-07 | 4.36E-05 | 1.52E-05 | - | 1.29E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 2.34E-06 | 1.63E-06 | 1.52E-05 | - | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 5.71E-06 | 1.53E-05 | 1.52E-05 | - | 1.71E-05 |
| IGROV | GI50 | 1.83E-06 | 5.02E-06 | 1.20E-06 | 1.86E-07 | 3.99E-06 | 3.07E-06 | 4.43E-06 | 1.19E-05 | 1.53E-05 | 6.48E-06 | 1.52E-05 | 6.42E-06 |
| | TGI | 5.90E-06 | 9.72E-06 | 3.01E-06 | 1.94E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.88E-05 | 7.54E-06 | 7.54E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| IGROV-ET | GI50 | 1.59E-06 | 1.94E-05 | 2.69E-06 | 6.78E-07 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.18E-05 | 1.52E-05 | 1.47E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 5.60E-06 | 3.33E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| SK-BR-3 | GI50 | 3.35E-06 | 5.84E-06 | 4.17E-07 | 1.23E-06 | 5.77E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 3.51E-06 | 7.89E-06 | 4.93E-06 |
| | TGI | 1.24E-05 | 1.67E-05 | 1.86E-06 | 3.58E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.23E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 5.47E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| MEL-28 | GI50 | 2.45E-06 | 5.88E-06 | 2.14E-06 | 2.62E-07 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 3.24E-06 | 1.52E-05 | 1.71E-05 |
| | TGI | 7.31E-06 | 1.30E-05 | 4.43E-06 | 4.71E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 8.27E-06 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.18E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| H-MEC-1 | GI50 | 1.59E-05 | 1.94E-05 | 3.81E-07 | 3.37E-08 | 7.60E-06 | 4.06E-06 | 3.41E-07 | 4.66E-06 | 5.43E-06 | 4.35E-06 | | 1.71E-05 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-08 | 7.60E-06 | 5.48E-06 | 2.31E-06 | 6.99E-06 | 8.39E-06 | 6.95E-06 | | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 7.42E-06 | 6.06E-06 | 1.05E-05 | 1.29E-05 | 1.11E-05 | | 1.71E-05 |
| A-549 | GI50 | 7.19E-06 | 1.94E-05 | 4.97E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| K-562 | GI50 | 5.26E-07 | 2.75E-06 | 1.63E-06 | 3.20E-06 | 6.42E-06 | 9.72E-07 | 1.54E-06 | 2.19E-06 | 2.94E-06 | 2.39E-06 | 9.59E-06 | 9.10E-06 |
| | TGI | 1.82E-06 | 1.94E-05 | 4.43E-06 | 6.86E-06 | 7.60E-06 | 1.48E-06 | 4.47E-06 | 3.53E-06 | 4.79E-06 | 4.24E-06 | 1.52E-05 | 1.71E-05 |
| | LC50 | 4.32E-06 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 2.26E-06 | 1.08E-05 | 5.73E-06 | 7.78E-06 | 7.54E-06 | 1.52E-05 | 1.71E-05 |
| PANC-1 | GI50 | 2.12E-06 | 1.31E-05 | 1.68E-06 | 4.47E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 5.14E-06 | 1.52E-05 | 1.05E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 5.65E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.47E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| HT-29 | GI50 | 1.55E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.28E-05 | 1.71E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| LOVO | GI50 | 5.70E-06 | 1.32E-05 | 2.28E-06 | 5.28E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 5.52E-07 | 1.52E-05 | 1.24E-05 |
| | TGI | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 3.27E-06 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| LOVO-DOX | GI50 | 2.84E-06 | 8.38E-06 | 5.63E-07 | 5.29E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 7.80E-06 |
| | TGI | 8.25E-06 | 1.94E-05 | 2.07E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| | LC50 | 1.59E-05 | 1.94E-05 | 9.20E-06 | 9.59E-06 | 7.60E-06 | 9.44E-06 | 1.08E-05 | 1.31E-05 | 1.53E-05 | 1.52E-05 | 1.52E-05 | 1.71E-05 |
| HELA | GI50 | - | - | - | - | - | - | - | - | - | - | 1.52E-05 | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | 1.52E-05 | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | 1.52E-05 | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - | - | - | 1.52E-05 | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | 1.52E-05 | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | 1.52E-05 | - |

| | | 106 | 107 | 108 | 109 | 110 | 111 | 112 | 113 | 114 | 115 | 116 | 117 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 2.15E-06 | 1.60E-05 | 4.76E-06 | 2.99E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.63E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 5.18E-06 | 1.60E-05 | 1.24E-05 | 1.54E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 4.29E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| LN-caP | GI50 | 6.06E-07 | 2.53E-06 | 4.09E-06 | 1.16E-06 | 4.09E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 4.82E-06 | 6.70E-07 | 1.08E-05 | 8.92E-06 |
| | TGI | 1.84E-06 | 1.01E-05 | 8.95E-06 | 1.99E-06 | 1.24E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.67E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 6.66E-06 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 3.87E-06 | 1.08E-05 | 8.92E-06 |
| SKOV-3 | GI50 | - | 1.60E-05 | 6.68E-06 | 2.49E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.10E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | - | 1.60E-05 | 1.59E-05 | 1.18E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.38E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | - | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 5.13E-06 | 1.08E-05 | 8.92E-06 |
| IGROV | GI50 | 2.11E-06 | 1.08E-05 | 2.50E-06 | 1.80E-06 | 8.11E-06 | 9.99E-06 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.07E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 5.21E-06 | 1.60E-05 | 6.36E-06 | 6.08E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.58E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 6.26E-06 | 1.08E-05 | 8.92E-06 |
| IGROV-ET | GI50 | 1.09E-05 | 1.60E-05 | 6.64E-06 | 9.67E-06 | 8.57E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.70E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 5.38E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| SK-BR-3 | GI50 | 1.16E-06 | 1.60E-05 | 4.45E-06 | 3.45E-06 | 1.30E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.87E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 4.15E-06 | 1.60E-05 | 1.16E-05 | 8.10E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 3.75E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.90E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.53E-06 | 1.08E-05 | 8.92E-06 |
| MEL-28 | GI50 | 2.61E-06 | 1.60E-05 | 4.29E-06 | 8.85E-07 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.45E-06 | 1.08E-05 | 8.92E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 8.55E-06 | 1.60E-05 | 9.16E-06 | 2.57E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.65E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.08E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 4.83E-06 | 1.08E-05 | 8.92E-06 |
| H-MEC-1 | GI50 | - | 5.26E-06 | 6.10E-06 | 9.17E-07 | 3.54E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 2.05E-06 | 2.13E-07 | 1.08E-05 | 8.92E-06 |
| | TGI | - | 8.26E-06 | 1.59E-05 | 1.99E-05 | 6.10E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 4.09E-06 | 4.52E-07 | 1.08E-05 | 8.92E-06 |
| | LC50 | - | 1.30E-05 | 1.59E-05 | 1.99E-05 | 1.05E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.96E-06 | 1.08E-05 | 8.92E-06 |
| A-549 | GI50 | 1.62E-06 | 1.60E-05 | 6.28E-06 | 5.94E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.65E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 8.85E-06 | 1.60E-05 | 1.59E-05 | 1.41E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 3.11E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 5.87E-06 | 1.08E-05 | 8.92E-06 |
| K-562 | GI50 | 1.53E-06 | 2.30E-06 | 6.53E-07 | 4.25E-07 | 1.91E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 5.36E-07 | 1.08E-05 | 8.92E-06 |
| | TGI | 5.06E-06 | 4.27E-06 | 2.06E-06 | 1.99E-05 | 3.27E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.47E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 7.93E-06 | 3.36E-06 | 1.99E-05 | 5.56E-06 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| PANC-1 | GI50 | 3.71E-06 | 1.60E-05 | 5.86E-06 | 5.70E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.47E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| HT-29 | GI50 | 1.64E-06 | 1.60E-05 | 1.31E-05 | 4.81E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 2.92E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 5.17E-06 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 6.46E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| LOVO | GI50 | 3.98E-06 | 1.60E-05 | 5.61E-06 | 9.17E-07 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.03E-07 | 1.08E-05 | 8.92E-06 |
| | TGI | 1.09E-05 | 1.60E-05 | 1.37E-05 | 4.07E-06 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.82E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 4.41E-06 | 1.08E-05 | 8.92E-06 |
| LOVO-DOX | GI50 | 1.09E-05 | 1.60E-05 | 5.07E-06 | 5.64E-06 | 1.59E-05 | 1.37E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 1.76E-06 | 1.08E-05 | 8.92E-06 |
| | TGI | 1.09E-05 | 1.60E-05 | 1.04E-05 | 1.35E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 4.78E-06 | 1.08E-05 | 8.92E-06 |
| | LC50 | 1.09E-05 | 1.60E-05 | 1.59E-05 | 1.99E-05 | 1.59E-05 | 1.67E-05 | 1.08E-05 | 8.06E-06 | 5.97E-06 | 7.78E-06 | 1.08E-05 | 8.92E-06 |
| HELA | GI50 | 1.51E-06 | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | 4.37E-06 | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | 1.09E-05 | - | - | - | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | 5.09E-06 | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | 1.09E-05 | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | 1.09E-05 | - | - | - | - | - | - | - | - | - | - | - |

| | | 118 | 119 | 120 | 121 | 122 | 123 | 124 | 125 | 126 | 127 | 128 | 129 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.60E-06 | 1.57E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.65E-06 | 8.90E-06 | 3.71E-06 | 2.53E-06 | 8.01E-06 | 1.33E-06 | 8.87E-06 |
| | TGI | 3.00E-06 | 3.73E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 5.28E-06 | 8.90E-06 | 7.85E-06 | 6.49E-06 | 9.16E-06 | 2.48E-06 | 8.87E-06 |
| | LC50 | 5.64E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 4.62E-06 | 8.87E-06 |
| LN-caP | GI50 | 9.87E-07 | 3.55E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 1.30E-06 | 8.90E-06 | 7.85E-06 | 1.25E-06 | 9.16E-06 | 1.26E-06 | 8.87E-06 |
| | TGI | 2.16E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.62E-06 | 8.90E-06 | 7.85E-06 | 2.76E-06 | 9.16E-06 | 2.69E-06 | 8.87E-06 |
| | LC50 | 4.76E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 5.27E-06 | 8.90E-06 | 7.85E-06 | 6.04E-06 | 9.16E-06 | 5.71E-06 | 8.87E-06 |
| SKOV-3 | GI50 | 2.02E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.61E-06 | 8.90E-06 | 7.85E-06 | 3.48E-06 | 9.16E-06 | - | 8.87E-06 |
| | TGI | 4.08E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 4.57E-06 | 8.90E-06 | 7.85E-06 | 6.98E-06 | 9.16E-06 | - | 8.87E-06 |
| | LC50 | 8.22E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 8.02E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | - | 8.87E-06 |
| IGROV | GI50 | 9.70E-07 | 3.21E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.02E-06 | 8.90E-06 | 7.85E-06 | 2.26E-06 | 9.16E-06 | 6.39E-07 | 8.87E-06 |
| | TGI | 2.30E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 4.49E-06 | 8.90E-06 | 7.85E-06 | 5.32E-06 | 9.16E-06 | 1.98E-06 | 8.87E-06 |
| | LC50 | 5.47E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.26E-05 | 9.16E-06 | 5.70E-06 | 8.87E-06 |
| IGROV-ET | GI50 | 8.76E-07 | 3.37E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 5.99E-06 | 8.90E-06 | 7.85E-06 | 3.88E-06 | 9.16E-06 | 6.89E-07 | 8.87E-06 |
| | TGI | 2.33E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 7.87E-06 | 9.16E-06 | 2.26E-06 | 8.87E-06 |
| | LC50 | 6.17E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 7.59E-06 | 8.87E-06 |
| SK-BR-3 | GI50 | 6.39E-07 | 1.02E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.99E-06 | 8.90E-06 | 7.85E-06 | 2.11E-06 | 9.16E-06 | - | 8.87E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 2.04E-06 | 3.44E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 6.94E-06 | 8.90E-06 | 7.85E-06 | 5.36E-06 | 9.16E-06 | - | 8.87E-06 |
| | LC50 | 6.25E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-06 | 9.16E-06 | - | 8.87E-06 |
| MEL-28 | GI50 | 1.65E-06 | 2.67E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.10E-06 | 8.90E-06 | 7.85E-06 | 2.93E-06 | 9.16E-06 | 1.57E-06 | 8.87E-06 |
| | TGI | 3.00E-06 | 7.10E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 3.86E-06 | 8.90E-06 | 7.85E-06 | 5.27E-06 | 9.16E-06 | 3.03E-06 | 8.87E-06 |
| | LC50 | 5.49E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 7.10E-06 | 8.90E-06 | 7.85E-06 | 9.48E-06 | 9.16E-06 | 5.86E-06 | 8.87E-06 |
| H-MEC-1 | GI50 | 1.45E-06 | 1.38E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 1.74E-06 | 2.40E-06 | 2.29E-06 | 7.46E-07 | 2.55E-06 | 1.53E-06 | 3.46E-06 |
| | TGI | 3.06E-06 | 3.88E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 3.18E-06 | 4.47E-06 | 4.48E-06 | 2.25E-06 | 4.71E-06 | 3.16E-06 | 8.87E-06 |
| | LC50 | 6.45E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 5.80E-06 | 8.30E-06 | 7.85E-06 | 6.46E-06 | 8.72E-06 | 6.53E-06 | 8.87E-06 |
| A-549 | GI50 | 1.80E-06 | 1.41E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 3.53E-06 | 8.90E-06 | 7.85E-06 | 2.98E-06 | 9.16E-06 | 1.61E-06 | 8.87E-06 |
| | TGI | 3.55E-06 | 3.16E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.50E-06 | 8.90E-06 | 7.85E-06 | 5.74E-06 | 9.16E-06 | 3.23E-06 | 8.87E-06 |
| | LC50 | 6.99E-06 | 7.08E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 2.25E-06 | 9.16E-06 | 6.45E-06 | 8.87E-06 |
| K-562 | GI50 | 1.17E-06 | 2.72E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 1.66E-06 | 8.90E-06 | 7.85E-06 | 2.15E-06 | 9.16E-06 | 1.11E-06 | 8.87E-06 |
| | TGI | 2.77E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 3.70E-06 | 8.90E-06 | 7.85E-06 | 4.32E-06 | 9.16E-06 | 2.98E-06 | 8.87E-06 |
| | LC50 | 6.57E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 8.18E-06 | 8.90E-06 | 7.85E-06 | 8.69E-06 | 9.16E-06 | 8.01E-06 | 8.87E-06 |
| PANC-1 | GI50 | 1.08E-06 | 4.69E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.68E-06 | 8.90E-06 | 7.85E-06 | 2.19E-06 | 9.16E-06 | 8.88E-07 | 8.87E-06 |
| | TGI | 2.40E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 7.42E-06 | 8.90E-06 | 7.85E-06 | 6.57E-06 | 9.16E-06 | 2.31E-06 | 8.87E-06 |
| | LC50 | 5.35E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 5.99E-06 | 8.87E-06 |
| HT-29 | GI50 | 1.92E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.58E-06 | 8.90E-06 | 7.85E-06 | 3.00E-06 | 9.16E-06 | 1.95E-06 | 8.87E-06 |
| | TGI | 3.56E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 5.73E-06 | 8.90E-06 | 7.85E-06 | 9.22E-06 | 9.16E-06 | 3.54E-06 | 8.87E-06 |
| | LC50 | 6.59E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 6.44E-06 | 8.87E-06 |
| LOVO | GI50 | 1.35E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 2.18E-06 | 8.90E-06 | 7.85E-06 | 2.56E-06 | 9.16E-06 | 8.54E-07 | 8.87E-06 |
| | TGI | 2.70E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 4.46E-06 | 8.90E-06 | 7.85E-06 | 5.68E-06 | 9.16E-06 | 1.92E-06 | 8.87E-06 |
| | LC50 | 5.43E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.11E-06 | 8.90E-06 | 7.85E-06 | 1.26E-05 | 9.16E-06 | 4.30E-06 | 8.87E-06 |
| LOVO-DOX | GI50 | 4.50E-07 | 1.69E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 4.03E-07 | 8.87E-06 |
| | TGI | 1.30E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 1.49E-06 | 8.87E-06 |
| | LC50 | 3.86E-06 | 7.60E-06 | 7.87E-06 | 8.04E-06 | 9.11E-06 | 9.73E-06 | 8.90E-06 | 7.85E-06 | 1.29E-05 | 9.16E-06 | 4.66E-06 | 8.87E-06 |
| HELA | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |

| | | 130 | 131 | 132 | 133 | 134 | 135 | 136 | 137 | 138 | 139 | 140 | 141 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.31E-06 | 8.86E-06 | 2.88E-06 | 7.77E-06 | 2.12E-06 | 1.60E-06 | 3.59E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.47E-06 | 3.78E-06 | 6.96E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| LN-caP | GI50 | 1.31E-06 | 8.86E-06 | 5.89E-06 | 7.77E-06 | 4.58E-07 | 7.83E-07 | 1.42E-06 | 2.87E-06 | 7.73E-06 | 9.71E-06 | 9.15E-06 | 3.35E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 1.34E-06 | 2.02E-06 | 6.10E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 6.83E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.16E-06 | 4.91E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| SKOV-3 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 7.39E-07 | 2.10E-06 | 4.54E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 1.85E-06 | 4.68E-06 | 8.83E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.26E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| IGROV | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 9.43E-07 | 5.86E-07 | 5.35E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 3.95E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 2.48E-06 | 1.98E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 6.50E-06 | 6.33E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| IGROV-ET | GI50 | 1.31E-06 | 8.86E-06 | 3.64E-06 | 7.77E-06 | 4.82E-07 | 5.79E-07 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 4.15E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 2.14E-06 | 2.61E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 7.58E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| SK-BR-3 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 2.10E-06 | 1.67E-06 | 5.71E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.34E-06 | 5.00E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| MEL-28 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 1.73E-06 | 3.34E-06 | 4.62E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 3.23E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 6.04E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| H-MEC-1 | GI50 | 1.31E-06 | 3.61E-06 | 4.37E-06 | 7.77E-06 | 2.13E-06 | 1.07E-06 | 8.04E-07 | 1.40E-06 | 2.54E-06 | 3.51E-06 | 4.00E-06 | 2.47E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 6.51E-06 | 6.82E-06 | 2.65E-06 | 4.37E-06 | 4.77E-06 | 7.05E-06 | 9.15E-06 | 3.81E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 7.57E-06 | 7.19E-06 | 8.96E-06 | 9.71E-06 | 9.15E-06 | 5.87E-06 |
| A-549 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 2.55E-06 | 2.11E-06 | 6.16E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.93E-06 | 5.53E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| K-562 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 5.71E-07 | 1.15E-06 | 1.26E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-08 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.93E-06 | 4.82E-06 | 8.31E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| PANC-1 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 2.17E-06 | 2.69E-06 | 8.37E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.53E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| HT-29 | GI50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 2.85E-06 | 3.80E-06 | 6.49E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.81E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| LOVO | GI50 | 1.31E-06 | 8.86E-06 | 3.00E-06 | 7.77E-06 | 2.05E-06 | 1.46E-06 | 6.61E-06 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 4.21E-06 | 3.97E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 8.67E-06 | 8.76E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| LOVO-DOX | GI50 | 1.31E-06 | 8.86E-06 | 4.21E-06 | 7.77E-06 | 5.19E-07 | 1.60E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | TGI | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 1.99E-06 | 3.57E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| | LC50 | 1.31E-06 | 8.86E-06 | 6.98E-06 | 7.77E-06 | 7.79E-06 | 7.98E-06 | 1.31E-05 | 7.19E-06 | 9.56E-06 | 9.71E-06 | 9.15E-06 | 7.59E-06 |
| HELA | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |

| | | 142 | 143 | 144 | 145 | 146 | 147 | 148 | 149 | 150 | 151 | 152 | 153 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 8.31E-06 | 4.00E-06 | 4.90E-06 | 2.46E-06 | 8.76E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 5.57E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.94E-06 | 8.76E-06 |
| LN-caP | GI50 | 4.58E-06 | 9.45E-06 | 2.53E-06 | 1.06E-05 | 8.78E-06 | 2.12E-06 | 2.58E-06 | 1.95E-06 | 1.73E-06 | 1.82E-06 | 2.13E-06 | 3.25E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 5.57E-06 | 4.69E-06 | 3.92E-06 | 4.44E-06 | 4.40E-06 | 8.31E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.13E-06 | 8.76E-06 |
| SKOV-3 | GI50 | 1.55E-06 | 9.45E-06 | 6.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 6.16E-06 | 6.69E-06 | 1.88E-06 | 2.93E-06 | 3.84E-06 | 4.73E-06 |
| | TGI | 2.80E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 4.61E-06 | 6.10E-06 | 6.57E-06 | 8.76E-06 |
| | LC50 | 5.04E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.94E-06 | 8.76E-06 |
| IGROV | GI50 | 9.02E-06 | 9.45E-06 | 8.75E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 6.97E-08 | 2.79E-06 | 1.55E-06 | 1.12E-08 | 2.27E-06 | 2.90E-06 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 3.84E-07 | 5.11E-06 | 3.26E-06 | 3.81E-08 | 4.29E-06 | 5.77E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 2.71E-06 | 9.40E-06 | 6.89E-06 | 2.89E-07 | 8.15E-06 | 8.76E-06 |
| IGROV-ET | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 4.76E-06 | 4.40E-06 | 1.25E-06 | 2.88E-06 | 2.24E-06 | 5.34E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.05E-05 | 9.54E-06 | 3.76E-06 | 6.74E-06 | 4.32E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 8.35E-06 | 8.76E-06 |
| SK-BR-3 | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 4.33E-06 | 3.65E-06 | 2.25E-06 | 3.05E-06 | 2.82E-06 | 5.03E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 9.95E-06 | 9.54E-06 | 5.56E-06 | 6.93E-06 | 5.95E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.94E-06 | 8.76E-06 |
| MEL-28 | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 5.35E-06 | 4.28E-06 | 3.10E-06 | 4.23E-06 | 5.76E-08 | 8.76E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 2.10E-07 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 7.34E-07 | 8.76E-06 |
| H-MEC-1 | GI50 | 2.35E-06 | 5.75E-06 | 3.02E-06 | 8.91E-06 | 5.21E-06 | 1.44E-06 | - | - | - | - | - | - |
| | TGI | 4.10E-04 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 4.29E-06 | - | - | - | - | - | - |
| | LC50 | 7.17E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | - | - | - | - | - | - |
| A-549 | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 4.94E-06 | 4.12E-06 | 2.88E-06 | 2.95E-06 | 2.99E-06 | 4.05E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 8.28E-06 | 6.04E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.94E-06 | 8.76E-06 |
| K-562 | GI50 | 1.42E-06 | 9.45E-06 | 5.39E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 3.93E-06 | 4.22E-06 | 1.56E-06 | 2.44E-06 | 1.97E-06 | 4.25E-06 |
| | TGI | 2.04E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 8.64E-06 | 8.62E-06 | 3.40E-06 | 5.10E-06 | 4.02E-06 | 8.76E-06 |
| | LC50 | 2.94E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 7.40E-06 | 9.28E-06 | 8.21E-06 | 8.76E-06 |
| PANC-1 | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 3.07E-06 | 4.27E-06 | 2.65E-06 | 3.82E-06 | 2.30E-06 | 8.10E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 5.12E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.94E-06 | 8.76E-06 |
| HT-29 | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 7.19E-06 | 7.73E-06 | 6.79E-06 | 6.98E-06 | 2.77E-06 | 8.76E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 5.13E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 9.49E-06 | 8.76E-06 |
| LOVO | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 5.59E-06 | 3.53E-06 | 4.13E-06 | 2.09E-06 | 8.76E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 3.94E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 7.42E-06 | 8.76E-06 |
| LOVO-DOX | GI50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 6.91E-06 | 3.63E-06 | 9.28E-06 | 2.44E-06 | 8.76E-06 |
| | TGI | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 4.29E-06 | 8.76E-06 |
| | LC50 | 9.02E-06 | 9.45E-06 | 9.10E-06 | 1.06E-05 | 8.78E-06 | 9.96E-06 | 1.06E-05 | 9.54E-06 | 8.45E-06 | 9.28E-06 | 7.59E-06 | 8.76E-06 |
| HELA | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - | - | - | - | - |

| | | 154 | 155 | 156 | 157 | 158 | 159 | 160 | 161 |
|---|---|---|---|---|---|---|---|---|---|
| DU-145 | GI50 | 1.08E-05 | 1.08E-05 | 3.34E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| LN-caP | GI50 | 4.29E-06 | 4.34E-06 | 4.63E-07 | - | - | - | - | - |
| | TGI | 9.58E-06 | 1.08E-05 | 2.23E-06 | - | - | - | - | - |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | - | - | - | - | - |
| SKOV-3 | GI50 | 7.73E-06 | 1.08E-05 | 6.17E-06 | 9.67E-06 | 4.91E-06 | 8.55E-06 | 6.68E-06 | 9.65E-06 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | TGI | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| IGROV | GI50 | 4.60E-06 | 6.33E-06 | 4.19E-07 | 9.67E-06 | 2.40E-06 | 4.26E-06 | 3.50E-06 | 3.95E-06 |
| | TGI | 1.02E-05 | 1.08E-05 | 3.79E-06 | 9.67E-06 | 4.14E-06 | 8.06E-06 | 7.05E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| IGROV-ET | GI50 | 4.33E-06 | 6.44E-06 | 3.81E-07 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 6.43E-06 | 5.00E-06 |
| | TGI | 9.71E-06 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| SK-BR-3 | GI50 | - | - | - | 2.25E-06 | 1.95E-06 | 2.04E-06 | 2.33E-06 | 3.26E-06 |
| | TGI | - | - | - | 8.96E-06 | 3.90E-06 | 4.32E-06 | 5.10E-06 | 6.36E-06 |
| | LC50 | - | - | - | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| MEL-28 | GI50 | 9.95E-06 | 1.08E-05 | 2.29E-06 | 9.67E-06 | 3.85E-06 | 7.88E-06 | 6.20E-06 | 9.65E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 7.26E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| H-MEC-1 | GI50 | - | - | - | - | 1.09E-07 | 6.35E-08 | 8.87E-06 | 9.65E-06 |
| | TGI | - | - | - | - | 1.42E-06 | 1.62E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | - | - | - | - | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| A-549 | GI50 | 1.08E-05 | 1.08E-05 | 5.66E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 8.33E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| K-562 | GI50 | 4.68E-06 | 6.89E-06 | 5.78E-07 | 3.57E-06 | 2.36E-06 | 5.05E-06 | 4.44E-06 | 4.79E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 3.89E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| PANC-1 | GI50 | 4.69E-06 | 1.08E-05 | 5.18E-06 | 9.67E-06 | 3.67E-06 | 5.45E-06 | 7.32E-06 | 9.65E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| HT-29 | GI50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| LOVO | GI50 | 1.08E-05 | 1.08E-05 | 3.47E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| LOVO-DOX | GI50 | 7.54E-06 | 1.08E-05 | 3.62E-06 | 9.67E-06 | 3.37E-06 | 8.55E-06 | 5.13E-06 | 9.65E-06 |
| | TGI | 1.08E-05 | 1.08E-05 | 7.78E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| | LC50 | 1.08E-05 | 1.08E-05 | 9.85E-06 | 9.67E-06 | 6.19E-06 | 8.55E-06 | 8.87E-06 | 9.65E-06 |
| HELA | GI50 | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - |
| HELA-APL | GI50 | - | - | - | - | - | - | - | - |
| | TGI | - | - | - | - | - | - | - | - |
| | LC50 | - | - | - | - | - | - | - | - |